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 * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

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L1       STRUCTURE UPLOADED

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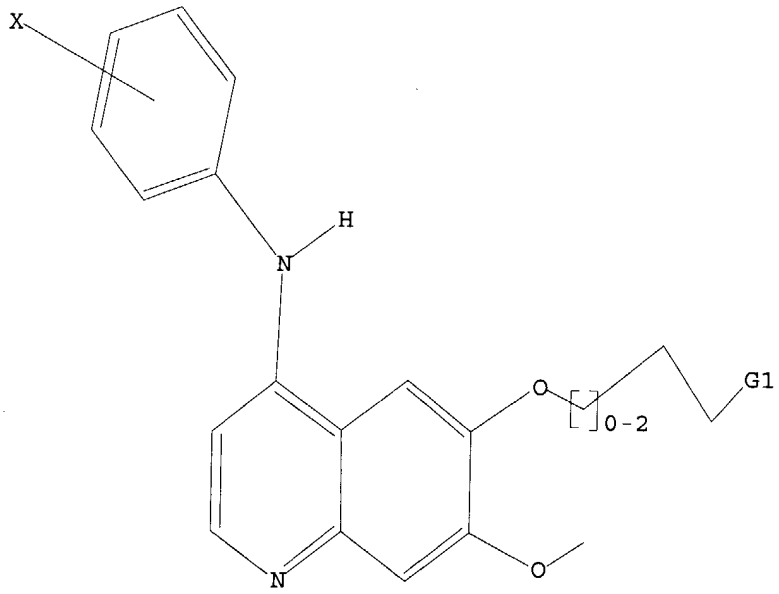


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G1 N,P


Structure attributes must be viewed using STN Express query preparation.


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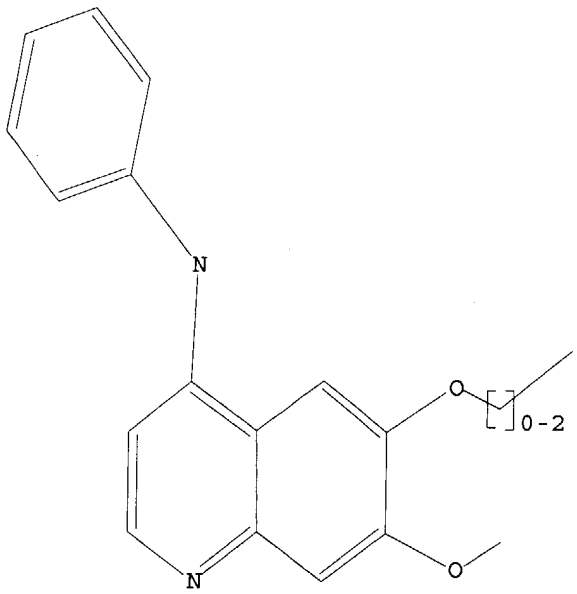

G1 N,P

Structure attributes must be viewed using STN Express query preparation.

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L5          1106 SEA SSS FUL L4

=> file ca

=> s l5
L6            47 L5

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L6 ANSWER 1 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 141:207223 CA

TITLE: Preparation of quinolines and quinazolines, in particular (quinazolin-4-yl)aminophenylethanone oximes, as anticancer agents

INVENTOR(S): Vedula, Manohar Sharma; Kattuboina, Venkata Adiseshu; Iqbal, Javed; Ramanujam, Rajagopalan; Rajagopal, Sriram; Mamidi, Naga Venkata Srinivasa Rao; Josyula, Ramanatham; Gutta, Madhusudhan

PATENT ASSIGNEE(S): Reddy's Laboratories Ltd., India

SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069145	A2	20040819	WO 2004-IB299	20040206

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MA108 A 20030207

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

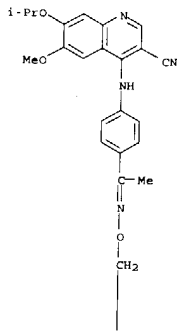
AB Title compds. I [wherein R1, R2 = H, halo, OH, NO2, CN, NH2, (un)substituted cyclo/ar/heteroar/heterocyclyl/alkyl, cyclo/alkoxy, acyl, acyloxy, hetero/aryl, aryloxy, alkylthio, arylthio, alkenyl, aroyl, heteroaryloxy, arylcarbonyl, CO2H and derivs., etc.; R3 = H, halo, OH, CN, NH2, CH2CN, (un)substituted cyclo/alkyl, ar/cyclo/alkoxy, hetero/aryl, aryloxy, acyl, CO2H and derivs., etc.; R4, R5, R6 = independently H, halo, OH, NO2, CN, NH2, (un)substituted ar/cyclo/alkyl, cyclo/alkoxy, hetero/aryl, acyl, CO2H and derivs., etc.; W = (un)substituted Ph, naphthyl, pyrrolyl, pyridyl, quinolinyl, benzofuryl, dihydrobenzofuryl, benzopyranyl, dihydrobenzopyranyl, indolyl, indolinyl, azaindolyl, azaindolinyl, pyrazolyl, benzothiazolyl, benzoxazolyl, and the like; Q = N, CH, C; Y = O, NH, CH2; X = (O)r; Z = (CH2)s; T = (CH2)t; U = (O)u; s, t = 0-5; r, u = 0-1; their pharmaceutically acceptable salts, and their geometrical isomers; with provisos] were prepd. as anticancer agents. A 3-step synthesis for quinazoline II is given. Selected I displayed potent antiproliferative activity in the human tumor lines with GI50 values at 48 h for MCF 7 (3-5 .mu.M), SW 620 (3-5 .mu.M), and H522 (3 .mu.M) and SKOV3 (2-7 .mu.M) cell lines.

IT **741275-79-6P**, 4-[[4-[1-[[(4-Fluorobenzyl)oxy]imino]ethyl]phenyl]amino]-7-isopropoxy 6-methoxyquinoline-3-carbonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; prepn. of quinolines and quinazolines, in particular (quinazolin-4-yl)aminophenylethanone oximes, as antitumor agents)

RN 741275-79-6 CA

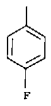
CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A



L6 ANSWER 1 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



L6 ANSWER 2 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 140:357180 CA

TITLE: 7-Alkoxy-4-phenylamino-3-quinolinecarbonitriles as Dual Inhibitors of Src and Abl Kinases

AUTHOR(S): Boschelli, Diane H.; Wang, Yanong D.; Johnson, Steve; Wu, Biqi; Ye, Fei; Sosa, Ana Carolina Barrios; Golas, Jennifer M.; Boschelli, Frank

CORPORATE SOURCE: Chemical and Screening Sciences and Oncology, Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Journal of Medicinal Chemistry (2004), 47(7), 1599-1601
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

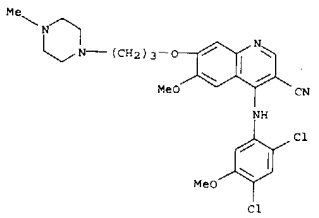
LANGUAGE: English

AB 7-Alkoxy-4-phenylamino-3-quinolinecarbonitriles were prepd. by several routes and are potent inhibitors of Src and Abl kinase activity.

IT **380843-75-4P**, SKI606
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of 7-alkoxy-4-phenylamino-3-quinolinecarbonitriles as inhibitors of Src and Abl kinases)

RN 380843-75-4 CA

CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:350577 CA
TITLE: Inhibition of src family kinases for the treatment of reperfusion injury related to revascularization
INVENTOR(S): Lorsordo, Douglas W.
PATENT ASSIGNEE(S): Caritas St. Elisabeth's Medical Center of Boston, Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032709	A2	20040422	WO 2003-US31430	20031003

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

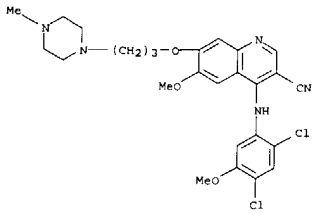
PRIORITY APPLN. INFO.: US 2002-416334P P 20021004

AB The invention provides methods for treating, preventing, or reducing reperfusion injury or post-pump syndrome by administering an inhibitor of vascular endothelial growth factor-mediated vascular permeability. The inhibitors of the invention include inhibitors of src family kinases.

IT **380843-75-4**, SKI-606
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(src family kinase inhibitors for treatment of reperfusion injury related to revascularization)

RN 380843-75-4 CA
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



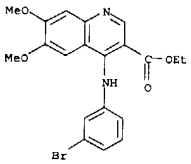
L6 ANSWER 4 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:314392 CA
TITLE: 3D-QSAR and docking studies on 4-anilinoquinazoline and 4-anilinoquinoline epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors
AUTHOR(S): Assefa, Haregewein; Kamath, Shantaram; Buolamwini, John K.
CORPORATE SOURCE: College of Pharmacy, Department of Pharmaceutical Sciences, University of Tennessee Health Sciences Center, Memphis, TN, 38163, USA
SOURCE: Journal of Computer-Aided Molecular Design (2003), 17(8), 475-493
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The overexpression and/or mutation of the epidermal growth factor receptor (EGFR) tyrosine kinase has been obsd. in many human solid tumors, and is under intense investigation as a novel anticancer mol. target. Comparative 3D-QSAR analyses using different alignments were undertaken employing comparative mol. field anal. (CoMFA) and comparative mol. similarity anal. (CoMSIA) for 122 anilinoquinazoline and 50 anilinoquinoline inhibitors of EGFR kinase. The SYBYL multifit alignment rule was applied to three different conformational templates, two obtained from a MacroModel Monte Carlo conformational search, and one from the bound conformation of erlotinib in complex with EGFR in the x-ray crystal structure. In addn., a flexible ligand docking alignment obtained with the GOLD docking program, and a novel flexible receptor-guided consensus dynamics alignment obtained with the DISCOVER program in the INSIGHTII modeling package were also investigated. 3D-QSAR models with q2 values up to 0.70 and r2 values up to 0.97 were obtained. Among the 4-anilinoquinazoline set, the q2 values were similar, but the ability of the different conformational models to predict the activities of an external test set varied considerably. In this regard, the model derived using the x ray crystallog. detd. bioactive conformation of erlotinib afforded the best predictive model. Electrostatic, hydrophobic and H-bond donor descriptors contributed the most to the QSAR models of the 4-anilinoquinazolines, whereas electrostatic, hydrophobic and H-bond acceptor descriptors contributed the most to the 4-anilinoquinoline QSAR, particularly the H bond acceptor descriptor. A novel receptor-guided consensus dynamics alignment has also been introduced for 3D-QSAR studies. This new alignment method may incorporate to some extent ligand-receptor induced fit effects into 3D-QSAR models.

IT **214470-41-4**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(3D-QSAR and docking studies on 4-anilinoquinazoline and 4-anilinoquinoline EGFR tyrosine kinase inhibitors)

RN 214470-41-4 CA
CN 3-Quinolinecarboxylic acid, 4-[(3-bromophenyl)amino]-6,7-dimethoxy-, ethyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 4 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:229401 CA
TITLE: Three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands
INVENTOR(S): Come, Jon H.; Becker, Frank; Kley, Nikolai A.; Reichel, Christoph
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S. Ser. No. 91,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

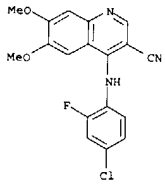
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004043388	A1	20040304	US 2002-234985		20020903
US 2003165873	A1	20030904	US 2002-91177		20020304
PRIORITY APPLN. INFO.:			US 2001-272932P	P	20010302
			US 2001 278233P	P	20010323
			US 2001-329437P	P	20011015
			US 2002-91177	A2	20020304

AB The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Prepn. of compds., e.g a methotrexate moiety linked by a polyethylene gycol moiety to dexamethasone, is described.

IT **214485-81-1D**, conjugates
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)

RN 214485 81-1 CA
CN 3-Quinolinecarbonitrile, 4-[(4-chloro-2-fluorophenyl)amino]-6,7-dimethoxy- (9CI) (CA INDEX NAME)

L6 ANSWER 5 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



L6 ANSWER 6 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:193052 CA
TITLE: Use of LCK inhibitors for treatment of immunological diseases
INVENTOR(S): Roth, Gerald Jurgen; Heckel, Armin; Walter, Rainer; Hilberg, Frank; Hauptmann, Rudolf; Ernst, Steffen; Stefanic, Martin; Colbatzky, Florian
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10237423	A1	20040219	DE 2002-10237423	20020816
WO 2004017948	A2	20040304	WO 2003-EP8890	20030811
WO 2004017948	A3	20040422		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

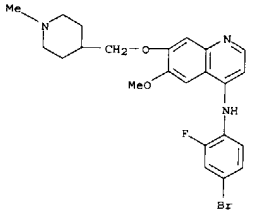
PRIORITY APPLN. INFO.: DE 2002-10237423 A 20020816

AB The invention discloses a method for treatment of immunol. diseases or pathol. conditions which contain an immunol. component, using certain LCK inhibitors, which already are known as kinase inhibitors for therapy in oncol., optionally in combination with one or more other medications selected from NSAIDs, steroids, DMARDs, immunosuppressants, biol. response modifiers, and antiinfectives. Also disclosed are pharmaceutical compns. which contain the LCK inhibitors as well as the other medications, and use of LCK inhibitors for prodn. of a pharmaceutical compn. for treatment of immunol. diseases or pathol. conditions which contain an immunol. component.

IT **660412-36-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LCK inhibitors for treatment of immunol. diseases, and use with other agents)

RN 660412-36-2 CA
CN 4-Quinolinamine, N-(4-bromo-2-fluorophenyl)-6-methoxy-7-[(1-methyl-4-piperidinyl)methoxy]- (9CI) (CA INDEX NAME)

L6 ANSWER 6 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



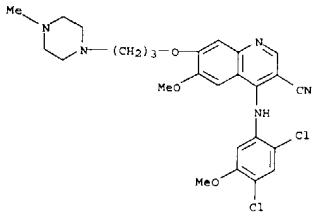
L6 ANSWER 7 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:42015 CA
TITLE: Investigation of the effect of varying the 4 anilino and 7-alkoxy groups of 3-quinolinecarbonitriles on the inhibition of Src kinase activity
AUTHOR(S): Boschelli, Diane H.; Ye, Fei; Wu, Biqi; Wang, Yanong D.; Barrios Sosa, Ana Carolina; Yaczko, Deanna; Powell, Dennis; Golas, Jennifer M.; Lucas, Judy; Boschelli, Frank
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, 401 N. Middletown Road, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(21), 3797-3800
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:42015

AB Several 7-alkoxy-4-anilino-3-quinolinecarbonitriles were synthesized and evaluated for Src kinase inhibitory activity. Optimal inhibition of both Src enzymic and cellular activity was seen with analogs having a 2,4-dichloro-5-methoxyaniline group at C-4. 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[(1-methyl-4-piperidinyl)methoxy]-3-quinolinecarbonitrile which has a 1-methylpiperidinemethoxy group at C-7, showed in vivo activity in a xenograft model. Compds. thus prepd. and tested included 4-(2,4-dichlorophenyl)-6,7-bis(2-methoxyethoxy)-3-quinolinecarbonitrile, 4-(2,4 dichloro-5-methoxyphenyl)-6,7-bis(2-methoxyethoxy)-3 quinolinecarbonitrile, 6,7-bis(2 methoxyethoxy)-4-(3,4,5-trimethoxyphenyl)-3-quinolinecarbonitrile, 4-[(2,4-dichlorophenyl)amino]-6-methoxy-7-(2-methoxyethoxy)-3-quinolinecarbonitrile.

IT **380843-75-4**, 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1 piperazinyl)propoxy]-3-quinolinecarbonitrile
RL: PAC (Pharmacological activity); BIOL (Biological study)
(SKI 606; investigation of effect of varying anilino and alkoxy groups of quinolinecarbonitriles on inhibition of Src kinase activity)

RN 380843-75-4 CA
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro 5-methoxyphenyl]amino]-6-methoxy-7 [3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

L6 ANSWER 7 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

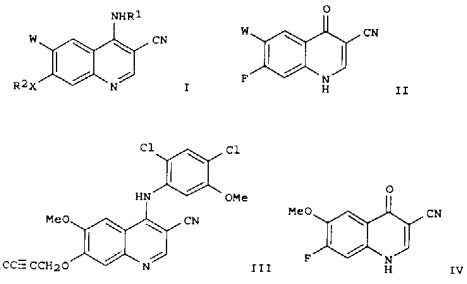


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:381383 CA
TITLE: Process for the preparation of 7-substituted 3 quinoline and 3-quinol-4 one carbonitriles via nucleophilic substitution
INVENTOR(S): Boschelli, Diane Harris; Wang, Yanong Daniel; Johnson, Steve Lawrence; Berger, Dan Maarten
PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003212276	A1	20031113	US 2003-425765	20030429
US 6780996	B2	20040824		
PRIORITY APPLN. INFO.:			US 2002 376456P P	20020430

OTHER SOURCE(S): MARPAT 139:381383
GI

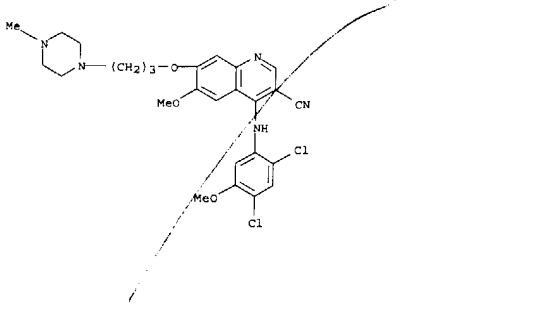


AB A new process for prepg. quinoline I, quinolone II, their intermediates and pharmaceutical salts, which are highly effective as inhibitors of protein kinases useful in the treatment of cancer, via nucleophilic substitution is provided [wherein X = O, S, NH, NR2'; W = H, OR3; R1 = (un)substituted alkyl, cycloalkyl, (un)substituted (fused) hetero/aryl; R2, R2', R3 = (un)substituted alk(en/yn)yl, or (un)substituted aryl, hetero(aryl/cyclyl) optionally attached to a linear chain which may contain O, S(O)m, or N-alkyl, or R2R2'N = (un)substituted heterocycle; m =

L6 ANSWER 8 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
0-2]. Specifically, 7-fluoro-4-oxo-1,4-dihydro-3-quinolinecarbonitriles were converted in three steps to 7-substituted 3-quinolinecarbonitriles by halogenation with POCl3 or POBr3, substitution of 4 halo-3-quinolinecarbonitrile intermediate with an amine R1NH2 in the presence of Py.bul.HCl, and substitution of 7-fluoro-3-quinolinecarbonitrile with a compd. of formula R2XH [wherein R1, R2, and X are defined as above]. III was prepd. by reacting IV (prepn. given) with POCl3 at reflux, N-alkylation of 2,4-dichloro-5-methoxy-aniline with the resulting 4-chloroquinoline-3-carbonitrile intermediate in 2-ethoxyethanol at 120.degree. in the presence of Py.bul.HCl, followed by addn. of 7-fluoroquinoline-3-carbonitrile to a preheated mixt. of 2 butyn-1-ol and Na and reaction overnight at 120.degree..

IT **380843-75-4P**, 4-[(2,4 Dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1 piperazinyl)propoxy]quinoline-3-carbonitrile
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(quinoline product; process for prepn. of 3-quinolinecarbonitriles via nucleophilic substitution)

RN 380843-75-4 CA
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl]propoxy]- (9CI) (CA INDEX NAME)



L6 ANSWER 9 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:364842 CA
TITLE: Process for the preparation of 7-substituted 3-quinoline and 3 quinol-4-one carbonitriles via nucleophilic substitution
INVENTOR(S): Boschelli, Diane Harris; Wang, Yanong Daniel; Johnson, Steven Lawrence; Berger, Dan Maarten
PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093241	A1	20031113	WO 2003-US13149	20030429

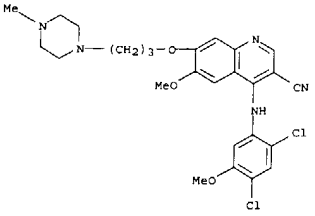
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-376456P P 20020430
OTHER SOURCE(S): CASREACT 139:364842; MARPAT 139:364842
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

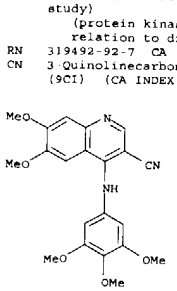
AB A new process for prepg. quinoline I, quinolone II, their intermediates and pharmaceutical salts, which are highly effective as inhibitors of protein kinases useful in the treatment of cancer, via nucleophilic substitution is provided [wherein X = O, S, NH, NR2'; W = H, OR3; R1 = (un)substituted alkyl, cycloalkyl, (un)substituted (fused) hetero/aryl; R2, R2', R3 = (un)substituted alk(en/yn)yl, or (un)substituted aryl, hetero(aryl/cyclyl) optionally attached to a linear chain which may contain O, S(O)m, or N-alkyl, or R2R2'N = (un)substituted heterocycle; m = 0-2]. Specifically, 7-fluoro-4-oxo 1,4-dihydro-3-quinolinecarbonitriles were converted in three steps to 7-substituted-3 quinolinecarbonitriles by halogenation with POCl3 or POBr3, substitution of 4-halo-3-quinolinecarbonitrile intermediate with an amine R1NH2 in the presence of Py.bul.HCl, and substitution of 7-fluoro-3-quinolinecarbonitrile with a compd. of formula R2XH [wherein R1, R2, and X are defined as above]. III

L6 ANSWER 9 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
was prepd. by reacting IV (prepn. given) with POCl3 at reflux, N-alkylation of 2,4-dichloro-5-methoxy-aniline with the resulting 4-chloroquinoline 3-carbonitrile intermediate in 2-ethoxyethanol at 120.degree. in the presence of Py.bul.HCl, followed by addn. of 7-fluoroquinoline-3-carbonitrile to a preheated mixt. of 2-butyn-1-ol and Na and reaction overnight at 120.degree..
IT **380843-75-4P**, 4-[(2,4-Dichloro 5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]quinoline-3-carbonitrile
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(quinoline product; process for prepn. of 3-quinolinecarbonitriles via nucleophilic substitution)
RN 380843-75-4 CA
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

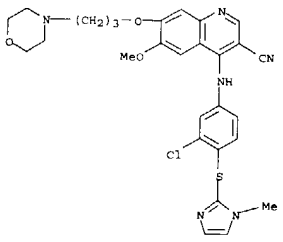
L6 ANSWER 10 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:358017 CA
TITLE: Kinases, Homology Models, and High Throughput Docking
AUTHOR(S): Diller, David J.; Li, Rixin
CORPORATE SOURCE: Pharmacopeia, Inc., Princeton, NJ, 08543-5350, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(22), 4638-4647
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With the many protein sequences coming from the genome sequencing projects, it is unlikely that the authors will ever have an at. resoln. structure of every relevant protein. With high throughput crystallog., however, the authors will soon have representative structures for the vast majority of protein families. Thus the drug discovery and design process will rely heavily on protein modeling to address issues such as designing combinatorial libraries for an entire class of targets and engineering genome-wide selectivity over a target class. In this study the authors assess the value of high throughput docking into homol. models. To do this the authors dock a database of random compds. seeded with known inhibitors into homol. models of six different kinases. In five of the six cases the known inhibitors were enriched by factors of 4-5 in the top 5% of the overall scored and ranked compds. Furthermore, in the same five cases the known inhibitors were enriched by factors of 2-3 in the top 5% of the scored and ranked known kinase inhibitors, thus showing that the homol. models can pick up some of the crucial selectivity information.
IT **319492-92-7D**, derivs.
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(protein kinases and homol. models and high throughput docking in relation to drug discovery and design)
RN 319492-92-7 CA
CN 3-Quinolinecarbonitrile, 6,7-dimethoxy-4-[(3,4,5-trimethoxyphenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:285653 CA
TITLE: Synthesis and evaluation of 4-Anilino-6,7-dialkoxy-3-quinolinecarbonitriles as inhibitors of kinases of the Ras-MAPK signaling cascade
AUTHOR(S): Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Bigi; Wissner, Allan; Boschelli, Diane H.; Floyd, M. Brawner; Zhang, Nan; Torres, Nancy; Levin, Jeremy; Du, Xuemei; Wojciechowicz, Donald; Discafani, Carolyn; Kohler, Constance; Kim, Steven C.; Feldberg, Larry R.; Collins, Karen; Mallon, Robert
CORPORATE SOURCE: Chemical Sciences, Wyeth Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(18), 3031-3034
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:285653
AB 4-[3-Chloro-4-(1-methyl-1H-imidazol-2-ylsulfanyl)]anilino-6,7-diethoxy-3-quinolinecarbonitrile (3) was identified as a MEK1 kinase inhibitor with exceptional activity against LoVo cells. The structure-activity relationships of the C-4 aniline substituents were explored, and water-solubilizing groups were added at the C-7 position to improve phys. properties. Secondary cellular assays revealed that a compd. possessing the appropriate aniline substituents inhibited MEK1 as well as MAPK phosphorylation, thereby acting as a dual inhibitor of the Ras-MAPK signaling cascade.
IT **263171-01-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and MEK1 kinase-inhibiting activity of 4-anilino 6,7-dialkoxy-3-quinolinecarbonitriles as antitumor agents)
RN 263171-01-3 CA
CN 3-Quinolinecarbonitrile, 4-[[3-chloro-4-[(1-methyl-1H-imidazol 2-yl)thio]phenyl]amino]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)

L6 ANSWER 11 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

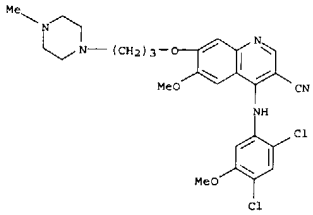
L6 ANSWER 12 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

L6 ANSWER 12 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:285650 CA
TITLE: Inhibition of Src kinase activity by 4-anilino-5,10-dihydro pyrimido[4,5-b]quinolines
AUTHOR(S): Boschelli, Diane H.; Powell, Dennis; Golas, Jennifer M.; Boschelli, Frank
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(18), 2977-2980
CODEN: BMCLE8; ISSN: 0960 894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:285650

AB 4-(2,4-Dichloro-5-methoxy)anilino-5,10-dihydropyrimido[4,5-b]quinolines are potent inhibitors of Src kinase and Src cellular activity while having no effect on Fyn cellular activity. The corresponding 4-(2,4-dichloro-5-methoxy)anilino-pyrimido[4,5-b]quinolines are much less effective Src inhibitors.

IT **380843-75-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and Src kinase-inhibiting activity of 4-anilino-5,10 dihydro-pyrimido[4,5-b]quinolines)

RN 380843-75-4 CA
CN 3-Quinolinecarbonitrile, 4-[(2,4 dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

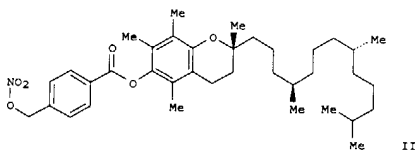


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 13 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:214237 CA
TITLE: Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases
INVENTOR(S): Scaramuzzino, Giovanni
PATENT ASSIGNEE(S): Italy
SOURCE: Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1336602	A1	20030820	EP 2002-425075	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			EP 2002-425075	20020213

GI



AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5, preferably 1; F is chosen among drugs such as .delta.-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1 M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = satd. or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a satd. or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, satd. or unsatd., linear or branched 1-21 carbon atom alkyl, satd. or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1 M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepd. For example, .alpha.-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl deriv. II. The compds. of

L6 ANSWER 13 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the prepn. of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

IT **586350-90-5P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

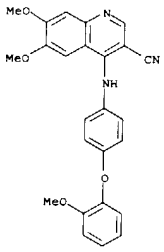
(prepn. of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586350-90-5 CA

CN 3-Quinolinecarbonitrile, 6,7-dimethoxy-4-[[4 (2-methoxyphenoxy)phenyl]amino]-, nitrate (9CI) (CA INDEX NAME)

CM 1

CRN 306997-79-5
CMF C25 H21 N3 O4



CM 2

CRN 7697-37-2
CMF H N O3

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

L6 ANSWER 14 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 139:85381 CA

TITLE: Preparation of quinoline-3-carbonitriles as antitumor agents

INVENTOR(S): Hennequin, Laurent Francois Andre; Gibson, Keith Hopkinson; Foote, Kevin Michael

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053960	A2	20030703	WO 2002-GB5518	20021205
WO 2003053960	A3	20030912		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

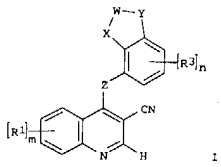
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-29099 A 20011205

OTHER SOURCE(S): MARPAT 139:85381

GI

L6 ANSWER 14 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



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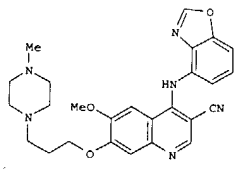


II

AB The title compds. [I; Z = O, S, SO, SO2, NR2, C(R2)2 (wherein R2 = H, alkyl); X, Y and W together with the carbon atoms to which they are attached form a 5 membered heterocyclic ring contg. 1 N atom and 1 O atom; m = 0-4; R1 = halo, CF3, CN, etc.; n = 0-3; R3 = halo, CF3, CN, etc.], useful in the manuf. of a medicament for use as anti-proliferative agents in the containment and/or treatment of solid tumor disease, were prepd. and formulated. Thus, reacting 4-chloro-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinoline-3-carbonitrile (prepn. given) with 4-amino-1,3-benzoxazole in the presence of NaH in DMF afforded 13% the quinoline-3-carbonitrile II. The compds. I tested had IC50 typically less than 0.5 .mu.M in assay to detect MEK inhibition.

IT **552867-31-9P**

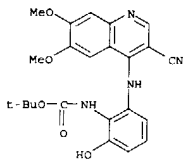
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of quinoline-3-carbonitriles as antitumor agents)

RN 552867-31-9 CA

CN Carbamic acid, [2-[(3-cyano-6,7-dimethoxy-4-quinolinyl)amino]-6-hydroxyphenyl]-, 1,1 dimethylethyl ester, hydrochloride (9CI) (CA INDEX NAME)

L6 ANSWER 14 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



●x HCl

L6 ANSWER 15 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 139:46567 CA

TITLE: SKI 606, a 4-Anilino-3-quinolinecarbonitrile Dual Inhibitor of Src and Abl Kinases, Is a Potent Antiproliferative Agent against Chronic Myelogenous Leukemia Cells in Culture and Causes Regression of K562 Xenografts in Nude Mice

AUTHOR(S): Golas, Jennifer M.; Arndt, Kim; Etienne, Carlo; Lucas, Judy; Nardin, Danielle; Gibbons, James; Frost, Philip; Ye, Fei; Boschelli, Diane H.; Boschelli, Frank

CORPORATE SOURCE: Departments of Oncology, Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Cancer Research (2003), 63(2), 375-381
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Constitutive tyrosine kinase activity of Bcr-Abl promotes proliferation and survival of chronic myelogenous leukemia (CML) cells. Inhibition of Bcr-Abl tyrosine kinase activity or signaling proteins activated by Bcr-Abl in CML cells blocks proliferation and causes apoptotic cell death.

The selective Abl kinase inhibitor, STI-571 (marketed as Gleevec), is toxic to CML cells in culture, causes regression of CML tumors in nude mice, and is currently used to treat CML patients. Here we describe a p.o. active, dual Src/Abl kinase inhibitor with potent antiproliferative activity against CML cells in culture. This 4-anilino 3-quinolinecarbonitrile (SKI-606) ablates tyrosine phosphorylation of Bcr-Abl in CML cells and of v-Abl expressed in fibroblasts. SKI-606 inhibits phosphorylation of cellular proteins, including STAT5, at concns.

that inhibit proliferation in CML cells. Phosphorylation of the autoactivation site of the Src family kinases Lyn and/or Hck is also reduced by treatment with SKI 606. Once daily oral administration of this

compd. at 100 mg/kg for 5 days causes complete regression of large K562 xenografts in nude mice.

IT **380843-75-4**, SKI 606

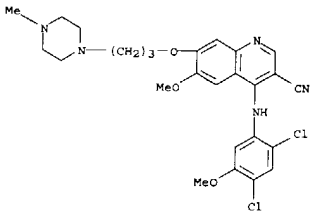
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Src and Abl kinase inhibitor SKI-606 is an antiproliferative agent against chronic myelogenous leukemia)

RN 380843-75-4 CA

CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

L6 ANSWER 15 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 16 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 138:237988 CA

TITLE: Syntheses and EGFR and HER 2 kinase inhibitory activities of 4-anilinoquinoline-3-carbonitriles: analogues of three important 4-anilinoquinazolines currently undergoing clinical evaluation as therapeutic antitumor agents

AUTHOR(S): Wissner, Allan; Brawner Floyd, M.; Rabindran, Sridhar K.; Nilakantan, Ramaswamy; Greenberger, Lee M.; Shen, Ru; Wang, Yu-Fen; Tsou, Hwei-Ru

CORPORATE SOURCE: Chemical Sciences and Oncology and Immunoinflammatory Research, Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2893-2897
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:237988

AB The syntheses and biol. evaluations of 4-anilinoquinoline-3-carbonitrile analogs of the three clin. lead 4-anilinoquinazolines Iressa, Tarceva, and

CI-1033 are described. The EGFR and HER-2 kinase inhibitory activities and the cell growth inhibition of the two series are compared with each other and with the clin. lead EKB-569. Similar activities are obsd. between these two series.

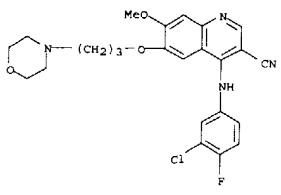
IT **214484-85-2P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn.s and EGFR and HER-2 kinase inhibitory activities of 4-anilinoquinoline-3-carbonitriles)

RN 214484-85-2 CA

CN 3-Quinolinecarbonitrile, 4-[(3-chloro-4 fluorophenyl)amino]-7-methoxy-6-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



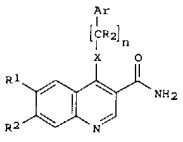
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 17 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:384765 CA
TITLE: Preparation of novel 4-anilinoquinoline-3-carboxamides as JAK3 kinase inhibitors
INVENTOR(S): Larsson, Joakim; Sjoe, Peter
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092571	A1	20021121	WO 2002 SE875	20020506
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1387830	A1	20040211	EP 2002-733657	20020506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300544	A	20040216	EE 2003-544	20020506
BR 2002009431	A	20040803	BR 2002-9431	20020506
NZ 529302	A	20040827	NZ 2002-529302	20020506
PRIORITY APPLN. INFO.:			SE 2001-1675 A	20010511
			WO 2002-SE875 W	20020506

OTHER SOURCE(S): MARPAT 137:384765
GI



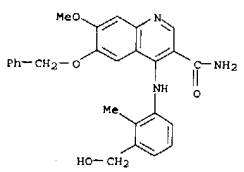
I

AB The title compds. [I; n = 0 1; X = NR3, O; Ar = (un)substituted Ph,

L6 ANSWER 17 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
indolyl, pyrazolyl, etc.; R = H, alkyl; R1, R2 = H, halo, NO2, etc.; or R1 and R2 are linked together as OCH2O or OCH2CH2O] which are JAK3 kinase inhibitors, useful in treating asthma, host vs. graft rejection/transplantation or rheumatoid arthritis, were prepd. E.g., a 7-step synthesis of I (X = NH; n = 0; Ar = 3-(hydroxymethyl)-2-methylphenyl; R1 = OCH2Ph; R2 = OMe), starting from 4-nitroguaiacol potassium salt, was given. The exemplified compds. I showed IC50 of < 25 .mu.M in JAK3 HTRF assay.

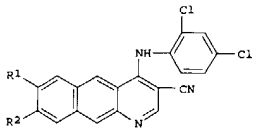
IT **476188-94-0P**, 6-(Benzyloxy)-4-[3-(hydroxymethyl)-2-methylanilino]-7-methoxy-3-quinolinecarboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of novel 4 anilinoquinoline-3-carboxamides as JAK3 kinase inhibitors)

RN 476188 94-0 CA
CN 3-Quinolinecarboxamide, 4-[[3-(hydroxymethyl) 2 methylphenyl]amino]-7-methoxy-6-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:93676 CA
TITLE: 4-Anilino-3-cyanobenzo[g]quinolines as Kinase Inhibitors
AUTHOR(S): Zhang, Nan; Wu, Biqi; Wissner, Allan; Powell, Dennis W.; Rabindran, Sridhar K.; Kohler, Constance; Boschelli, Frank
CORPORATE SOURCE: Chemical Sciences, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(3), 423-425
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



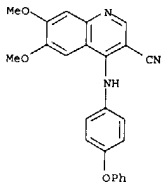
I

AB 4-Anilino-3-cyanobenzo[g]quinolines, e.g., I (R1 = R2 = MeO, OH; R1 = MeO, R2 = H; R1 = H, R2 = MeO) were prepd. as potent kinase inhibitors. Compared with their bicyclic 4-anilino-3-cyanoquinoline analogs, the tricyclic 4-anilino 3-cyanobenzo[g]quinolines are less active against EGF R kinase, equally active against MAPK kinase (MEK), and more active against Src kinase. For Src kinase inhibition, the best activity is obtained when both the 7- and 8-positions are substituted with alkoxy groups. Several of these kinase inhibitors show potent growth inhibitory activity in tumor cells.

IT **214487-04-4**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(4-anilinobenzo[g]quinoline-3-carbonitriles as kinase inhibitors)

RN 214487-04-4 CA
CN 3-Quinolinecarbonitrile, 6,7-dimethoxy-4-[(4-phenoxyphenyl)amino]- (9CI) (CA INDEX NAME)

L6 ANSWER 18 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:20303 CA
TITLE: Preparation of substituted quinolines as antitumor agents
INVENTOR(S): Boyle, Francis Thomas; Gibson, Keith Hopkinson; Foote, Kevin Michael
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044166	A1	20020606	WO 2001-GB4737	20011026
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002010714	A5	20020611	AU 2002-10714	20011026
EP 1337524	A1	20030827	EP 2001-978616	20011026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004514718	T2	20040520	JP 2002-546536	20011026
US 2004029898	A1	20040212	US 2003-415812	20030502

PRIORITY APPLN. INFO.: GB 2000-26744 A 20001102
GB 2000-26746 A 20001102
GB 2000-26747 A 20001102
WO 2001-GB4737 W 20011026

OTHER SOURCE(S): MARPAT 137:20303
GI

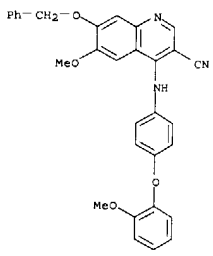
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [n = 0 or 1; Y = NH, O, S, or alkylamine; R5 = CN, F, Cl, or Br; R6 = (un)substituted -cycloalkyl, -pyridinyl, -pyrimidinyl, -Ph, etc.; R1, R2 and R4 independently = H, OH, halo, CN, NO2, F3C, alkyl, amine, alkylamine, dialkylamine, R7X1(CH2)x- wherein x = 0-3, R7 = H, (un)substituted hydrocarbyl or heterocyclyl and X1 = O, CH2, OCO, CO, S, SO, SO2, NR8CO, NR8CO2, CONR9, CO2NR9, SO2NR10, NR11 or NR11NR11 wherein R8, R9, R10 and R11 independently = H, alkyl or alkoxyalkyl; R3 = group of

L6 ANSWER 19 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
formula X1R12(OH)p where p = 1-2 and R12 = alkylene, alkenylene or alkynylene chain, optionally interposed with a heteroatom or heterocyclic ring with the provision that when R12 = alkylene, R12 must be interposed with a heteroatom or heterocyclic ring and at least one (OH)p is on the alkylene chain between X1 and the interposed heteroatom or heterocyclic ring; group of formula R7(CH2)yX1(CH2)x where y = 0-5 and (CH2)y is optionally interposed by an X1 group; group of formula X1alkyl where alkyl is substituted by one or more Cl and/or CN; heterocyclic ring, etc.], or a pharmaceutically acceptable salt, pro-drug or solvate thereof are prepd. and disclosed as antiproliferative agents. Thus, II was prepd. in eight steps from benzylchloroformate and 2-methoxy-5-nitroaniline. I were evaluated as inhibitors of MAPK pathway and exhibited IC50 values typically less than 0.5 .mu.M, e.g., II possessed an IC50 = 0.0013.mu.M. In cell proliferation assays, I had IC50 results typically less than 30.mu.M with II giving an IC50 of 1.3 .mu.M in HT29 human colon tumor cells. Methods for prevention of cancer comprising administering an effective amt. of compd. I are further claimed.

IT **306997-87-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn., inhibition of MAP kinase, and cellular antiproliferation activity of substituted quinolines as antitumor agents)

RN 306997-87-5 CA
CN 3-Quinolinecarbonitrile, 6-methoxy-4-[[4-(2-methoxyphenoxy)phenyl]amino]-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:369616 CA
TITLE: Preparation of 3-cyano-4-arylaminoquinolines as inhibitors of MAP kinase for use as antitumor agents
INVENTOR(S): Boyle, Francis Thomas; Gibson, Keith Hopkinson
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036570	A1	20020510	WO 2001-GB4733	20011025
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001095791	A5	20020515	AU 2001 95791	20011025
EP 1337513	A1	20030827	EP 2001-976523	20011025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517059	T2	20040610	JP 2002-539330	20011025

PRIORITY APPLN. INFO.: GB 2000-26745 A 20001102
GB 2000-26747 A 20001102
WO 2001 GB4733 W 20011025

OTHER SOURCE(S): MARPAT 136:369616
GI

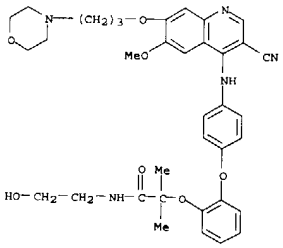
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I [R1, R2, R3, R4 independently H, HO, halogen, NC, O2N, F3C, (un)substituted C1-C3 alkyl, (un)substituted amino, satd. heterocyclyl contg. two heteroatoms; R5 = NC, F, Cl, Br; R6 = divalent C1-C5 alkenyl, C3-C7 cycloalkyl, or heteroaryl moiety; R7 = AR8; A = bond, O, CO, S, SO, SO2, (un)substituted aminocarbonyl, (un)substituted carbonylamino, (un)substituted sulfonylamino, (un)substituted aminosulfonyl, (un)substituted amino; R8 = C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl; R9 = (un)substituted C3-C7 divalent cycloalkyl; R10 = (un)substituted arylene, heteroarylene, heteroarylene N-oxide, C3-C10 cycloalkylene; X = amino, (C1-C6)alkylamino, O, S, CH2; Y = amino, (C1-C6)alkylamino, O, S; Z = (un)substituted alkyl, alkylene, alkynylene, O, CO, COO, S, SO, SO2, (un)substituted aminocarbonyl, carbonylamino, sulfonylamino, aminosulfonyl, amino; n = 0,1; m and p independently 0-3; alternatively, R10Z(CH2)pR6R7 can be replaced with a heteroaryl or heterocyclyl-2,3-fused

L6 ANSWER 20 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
Ph ring] were prepd. as inhibitors of MAP kinase for use as antitumor agents. E.g., 1-fluoro-4-nitrobenzene undergoes nucleophilic substitution with (2-hydroxyphenoxy)acetic acid followed by coupling of the acid with Me glycinate, redn. of the nitro group with Pd/C, and reaction of the ester with N-methylpiperazine to give the aminophenoxymethylcarbonylaminoa cetyl piperazine II. E.g., coupling of II with 4-chloro-6,7-dimethoxy-3-quinolinenitrile gave the example compd. III. Biol. data was obtained for selected compds. Selected compds. inhibited MAP kinase with IC50 < 0.5 .mu.M; for example, III gave an IC50 of 3.8 nM. In addn., selected compds. inhibited the proliferation of human colon cancer cells with IC50 < 30 .mu.M; for example, III gave an IC50 of 1 .mu.M.

IT **423179-48-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compds.; prepn. of 4-arylamino-3-cyanoquinolines as inhibitors of MAP kinase for potential use as antitumor agents)

RN 423179-48-0 CA
CN Propanamide, 2-[2-[4-[[3-cyano-6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinolinyl]amino]phenoxy]phenoxy] N-(2-hydroxyethyl)-2 methyl- (9CI) (CA INDEX NAME)

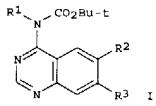


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:216752 CA
TITLE: Preparation of 4-aminoquinazolines as inhibitors of signal transduction mediated by tyrosine kinase
INVENTOR(S): Himmelsbach, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10040527	A1	20020228	DE 2000-10040527	20000818
PRIORITY APPLN. INFO.:			DE 2000-10040527	20000818

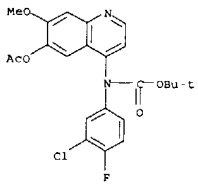
OTHER SOURCE(S): MARPAT 136:216752
GI



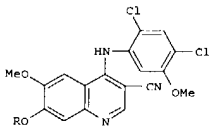
I

AB Title compds. [I; R1 = PhCH2, (substituted) Ph; R2 = OH, alkylcarbonyloxy, amino, NO2; R3 = H, F, Cl, Br, cycloalkoxy, cycloalkylalkoxy, (substituted) alkoxy], and stereoisomers and salts thereof are claimed. I were said to inhibit signal transduction mediated by tyrosine kinase.
IT **402472-94-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoquinazolines as inhibitors of signal transduction mediated by tyrosine kinase)
RN 402472-94-0 CA
CN Carbamic acid, [6-(acetyloxy)-7-methoxy-4 quinolinyl](3-chloro-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L6 ANSWER 21 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



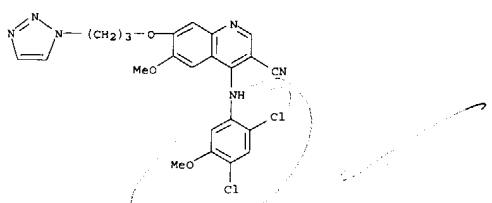
L6 ANSWER 22 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:37492 CA
TITLE: Optimization of 4-Phenylamino 3 quinolinecarbonitriles as Potent Inhibitors of Src Kinase Activity
AUTHOR(S): Boschelli, Diane H.; Ye, Fei; Wang, Yanong D.; Dutia, Minu; Johnson, Steve L.; Wu, Biqi; Miller, Karen; Powell, Dennis W.; Yaczko, Deanna; Young, Mairead; Tischler, Mark; Arndt, Kim; Discafani, Carolyn; Etienne, Carlo; Gibbons, Jay; Grod, Janet; Lucas, Judy; Weber, Jennifer M.; Boschelli, Frank
CORPORATE SOURCE: Chemical Sciences Discovery Analytical Chemistry and Oncology, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(23), 3965-3977
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:37492
GI



I

AB Subsequent to the discovery of 4-[(2,4-dichlorophenyl)amino]-6,7-dimethoxy-3-quinolinecarbonitrile as an inhibitor of Src kinase activity (IC50 = 30 nM), several addnl. analogs were prepd. Optimization of the C-4 anilino group led to I [R = Me]. Replacement of the methoxy group at C-7 with a 3-(morpholin-4-yl)propoxy group provided I [R = morpholinopropyl], resulting in increased inhibition of both Src kinase activity and Src-mediated cell proliferation. Analogs of I [R = morpholinopropyl] with other trisubstituted anilines at C-4 were also potent Src inhibitors, and the propoxy group was preferred over ethoxy, butoxy, or pentoxy. Replacement of the morpholine group with a 4-methylpiperazine group provided I [R = 4-methylpiperazinopropyl], which had an IC50 of 1.2 nM in the Src enzymic assay, an IC50 of 100 nM for the inhibition of Src-dependent cell proliferation and was selective for Src over non-Src family kinases. I [R = 4-methylpiperazinopropyl], which had higher 1 and 4 h plasma levels than I [R = 4-morpholinopropyl], effectively inhibited tumor growth in xenograft models.
IT **263150-07-8P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of 4-phenylamino-3-quinolinecarbonitriles as potent inhibitors of Src kinase activity)

L6 ANSWER 22 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
RN 263150-07-8 CA
CN 3 Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(1H-1,2,3-triazol-1-yl)propoxy] (9CI) (CA INDEX NAME)

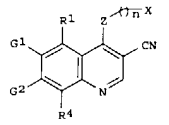


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

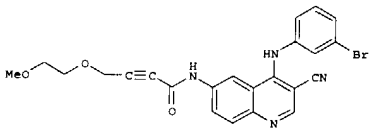
L6 ANSWER 23 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:272896 CA
TITLE: Preparation of substituted 3-cyanoquinolines as protein tyrosine kinases inhibitors
INVENTOR(S): Wissner, Allan; Tsou, Hwei-ru; Berger, Dan M.; Floyd, Middleton B., Jr.; Hamann, Philip R.; Zhang, Nan; Frost, Philip
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: U.S., 57 pp., Cont. of U.S. Ser. No. 405,868, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6297258	B1	20011002	US 2000-630270		20000801
PRIORITY APPLN. INFO.:			US 1998 150699P	P	19980929
			US 1999-405868	B1	19990924

OTHER SOURCE(S): MARPAT 135:272896
GI



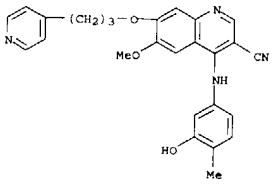
I



II

AB Title compds. I [X = cycloalkyl, pyridinyl, pyrimidinyl, etc.; Z = NH, O, S, NR; R = alkyl; G1, G2, R1, R4 = H, halo, alkyl, alkynyl, etc.; n = 0, 1], protein tyrosine kinase inhibitors, were prepd. Examples included 189

L6 ANSWER 23 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
compds. and 6 bioassays. E.g., II was prepd. by coupling the 4-(2-methoxyethoxy)but-2-ynoic acid with 6-amino-3-cyano-4-[(3-bromophenyl)amino]quinoline (i-BuOCOCl, N-methylmorpholine, THF, 0.degree.C, 3 h) in 32% yield after purifn. II had IC50 = 0.006 .mu.M for
EGFR kinase. I are useful as antineoplastic agents.
IT **263149-12-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyanoquinolines as protein tyrosine kinase inhibitors)
RN 263149-12-8 CA
CN 3-Quinolinecarbonitrile, 4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-[3-(4-pyridinyl)propoxy]-, hydrochloride (9CI) (CA INDEX NAME)



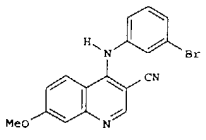
●x HCl

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 24 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:242152 CA
TITLE: Preparation of 4-anilinoquinoline-3-carbonitriles as colonic polyp inhibitors
INVENTOR(S): Frost, Philip; Discafani-Marro, Carolyn M.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068186	A2	20010920	WO 2001-US7068	20010306
WO 2001068186	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1263503	A2	20021211	EP 2001 918367	20010306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009165	A	20030422	BR 2001-9165	20010306
JP 2003526686	T2	20030909	JP 2001-566747	20010306
US 6384051	B1	20020507	US 2001-805070	20010313
NO 2002004356	A	20021112	NO 2002-4356	20020912
PRIORITY APPLN. INFO.:			US 2000-304198P	P 20000313
			US 2000-524196	A 20000313
			WO 2001-US7068	W 20010306

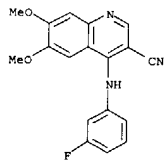
OTHER SOURCE(S): MARPAT 135:242152
GI



II

AB R(CH2)nZZ1CN [I; R = (un)substituted cycloalkyl, -Ph, -pyridinyl, -pyrimidinyl; Z = O, S, (alkyl)imino; Z1 = 5-8-(un)substituted quinoline-4,3-diyl; n = 0 or 1] were prepd. Thus, 3-(MeO)C6H4NH2 was cyclocondensed with NCC(:CHOEt)CO2Et and the chlorinated product aminated by 3-BrC6H4NH2 to give title compd. II. Data for biol. activity of 1

L6 ANSWER 24 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
prepd. I were given.
IT **214484-23-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-anilinoquinoline-3-carbonitriles as colonic polyp inhibitors)
RN 214484-23-8 CA
CN 3-Quinolinecarbonitrile, 4-[(3-fluorophenyl)amino]-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 25 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 135:235896 CA

TITLE: MEK (MAPKK) inhibitors. Part 2: structure-activity relationships of 4-anilino-3-cyano-6,7-dialkoxyquinolines

AUTHOR(S): Zhang, N.; Wu, B.; Eudy, N.; Wang, Y.; Ye, F.; Powell, D.; Wissner, A.; Feldberg, L. R.; Kim, S. C.; Mallon, R.; Kovacs, E. D.; Toral-Barza, L.; Kohler, C. A.

CORPORATE SOURCE: Chemical Sciences, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(11), 1407-1410
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

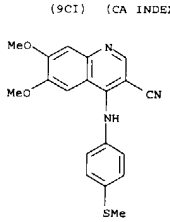
LANGUAGE: English

AB A series of 4-anilino-3-cyano-6,7-dialkoxyquinolines with different substituents attached to the 4-anilino group has been prepd. that are potent MEK (MAP kinase kinase) inhibitors. The best activity is obtained when a Ph or a thienyl group is attached to the para-position of the aniline through a hydrophobic linker, such as an oxygen, a sulfur, or a methylene group. The most active compds. show low nanomolar IC50's against MEK (MAP kinase kinase), and have potent growth inhibitory activity in LoVo cells (human colon tumor line).

IT **214486-41-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MEK (MAPKK) inhibitors and structure-activity relationships of 4-anilinocyanodialkoxyquinolines in relation to antitumor activity)

RN 214486-41-6 CA

CN 3-Quinolinecarbonitrile, 6,7-dimethoxy-4-[[4-(methylthio)phenyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

L6 ANSWER 26 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 135:226901 CA

TITLE: Preparation of 3-cyanoquinolines as protein tyrosine kinase inhibitors

INVENTOR(S): Wissner, Allan; Tsou, Hwei-ru; Berger, Dan M.; Floyd, Middleton B., Jr.; Hamann, Philip R.; Zhang, Nan; Salvati, Mark E.; Frost, Philip

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: U.S., 68 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

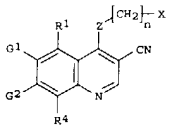
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6288082	B1	20010911	US 1999-406573	19990924
PRIORITY APPLN. INFO.:			US 1998-150693P P	19980929

OTHER SOURCE(S): MARPAT 135:226901

GI



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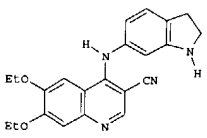


II

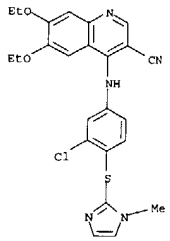
AB The title compds. [I; X = (un)substituted bicyclic aryl or bicyclic heteroaryl ring system of 8-12 atoms where the bicyclic heteroaryl ring contains 1 4 heteroatoms selected from N, O and S; Z = (un)substituted NH, O, S; G1, G2, R1, R4 = H, halo, alkyl, etc.; n = 0-1], useful as antineoplastic agents and in the treatment of polycystic kidney disease, were prepd. Thus, Me 2-amino-4,5-diethoxybenzoate was N-condensed with HCNMe2/POCl3 and the product cyclocondensed with MeCN to give, after POCl3 treatment, 4 chloro-6,7-diethoxyquinoline-3-carbonitrile which was aminated by 6-aminoindoline to give title compd II. Data for biol. activity (inhibition of EGFR kinase, KDR, Eck, Mek Erk) of I were given.

IT **263170-59-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-cyanoquinolines as protein tyrosine kinase inhibitors)

RN 263170-59-8 CA

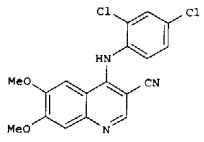
CN 3-Quinolinecarbonitrile, 4-[[3-chloro-4-[(1-methyl-1H-imidazol-2-yl)thio]phenyl]amino]-6,7-diethoxy- (9CI) (CA INDEX NAME)

L6 ANSWER 26 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 27 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:260864 CA
TITLE: Synthesis and Src kinase inhibitory activity of a series of 4-phenylamino-3-quinolinecarbonitriles
AUTHOR(S): Boschelli, Diane H.; Wang, Yanong D.; Ye, Fei; Wu, Biqi; Zhang, Nan; Dutia, Minu; Powell, Dennis W.; Wissner, Allan; Arndt, Kim; Weber, Jennifer M.; Boschelli, Frank
CORPORATE SOURCE: Chemical Sciences and Oncology, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(5), 822-833
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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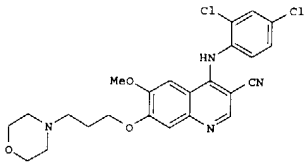
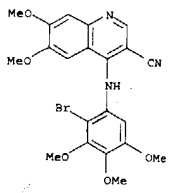


II

AB Screening of a directed compd. library in a yeast-based assay identified 4-[(2,4-dichlorophenyl)amino]-6,7-dimethoxy-3-quinolinecarbonitrile (I) as a Src inhibitor. An enzymic assay established that I was an ATP competitive inhibitor of the kinase activity of Src. We present here SAR data for I which shows that the aniline group at C-4, the carbonitrile group at C-3, and the alkoxy groups at C-6 and C-7 of the quinoline are crucial for optimal activity. Increasing the size of the C-2 substituent of the aniline at C-4 of I from chloro to bromo to iodo resulted in a corresponding increase in Src inhibition. Furthermore, replacement of the

L6 ANSWER 27 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
7-methoxy group of I with various 3-heteroalkylaminopropoxy groups provided increased inhibition of both Src enzymic and cellular activity. Compd. II, which contains a 3-morpholinopropoxy group, had an IC50 of 3.8 nM in the Src enzymic assay and an IC50 of 940 nM for the inhibition of Src-dependent cell proliferation.
IT **319492-80-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and Src kinase inhibitory activity of a series of 4-phenylamino-3-quinolinecarbonitriles)
RN 319492-80-3 CA
CN 3-Quinolinecarbonitrile, 4-[(2-bromo-3,4,5-trimethoxyphenyl)amino]-6,7-dimethoxy- (9CI) (CA INDEX NAME)



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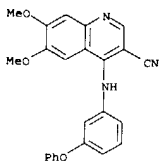
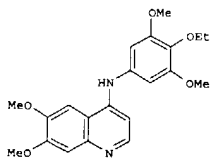
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:216794 CA
TITLE: Synthesis and Structure-Activity Relationships of 3-Cyano-4-(phenoxyanilino)quinolines as MEK (MAPKK) Inhibitors
AUTHOR(S): Zhang, N.; Wu, B.; Powell, D.; Wissner, A.; Floyd, M. B.; Kovacs, E. D.; Toral-Barza, L.; Kohler, C.
CORPORATE SOURCE: Chemical Sciences, Wyeth Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(24), 2825-2828
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 3-cyano-4-(phenoxyanilino)cyanoquinolines has been prepd. as MEK (MAP kinase kinase) inhibitors. The best activity is seen with alkoxy groups at both the 6- and 7-positions. The lead compds. show low nanomolar IC50's against MAP kinase kinase, and have potent inhibitory activity in tumor cells.
IT **214486-70-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structure-activity relationship of [(phenoxyphenyl]amino]quinolinecarbonitrile derivs. as mitogen-activated protein kinase (phosphorylating kinase) inhibitors)
RN 214486-70-1 CA
CN 3-Quinolinecarbonitrile, 6,7-dimethoxy-4-[(3-phenoxyphenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 29 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:100834 CA
TITLE: Inhibitors of Src tyrosine kinase: the preparation and structure-activity relationship of 4-anilino-3-cyanoquinolines and 4-anilinoquinazolines
AUTHOR(S): Wang, Yanong D.; Miller, Karen; Boschelli, Diane H.; Ye, Fei; Wu, Biqi; Floyd, M. Brawner; Powell, Dennis W.; Wissner, Allan; Weber, Jennifer M.; Boschelli, Frank
CORPORATE SOURCE: Chemical Sciences and Oncology, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(21), 2477-2480
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:100834
GI



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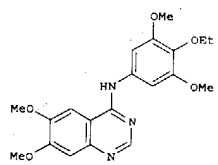
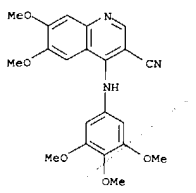


II

AB Src is a nonreceptor tyrosine kinase involved in signaling pathways that control proliferation, migration, and angiogenesis. Increased Src expression and activity are assocd. with an increase in tumor malignancy and poor prognosis. Several quinolines and quinazolines, e.g., I and II resp., were prepd. and identified as potent and selective inhibitors of Src kinase activity. Structure-activity relationships were examd. and revealed that the cyano group at C-3 and the NH linker at C-4 are required for good Src inhibitory activity.
IT **319492-92-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. and structure-activity relationship of anilinocyanoquinolines and anilinoquinazolines as inhibitors of Src tyrosine kinase)
RN 319492-92-7 CA
CN 3-Quinolinecarbonitrile, 6,7-dimethoxy-4-[(3,4,5-trimethoxyphenyl)amino]- (9CI) (CA INDEX NAME)

L6 ANSWER 29 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 30 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:362712 CA
TITLE: Preparation of quinoline derivatives as inhibitors of MEK enzymes
INVENTOR(S): Boyle, Francis Thomas; Gibson, Keith Hopkinson; Poyser, Jeffrey Philip; Turner, Paul
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

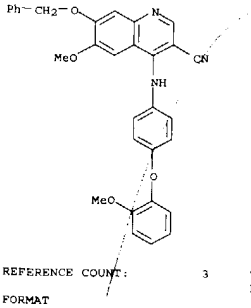
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068201	A1	20001116	WO 2000-GB1697	20000503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1178967	A1	20020213	EP 2000-927491	20000503
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103186	T2	20020422	TR 2001-200103186	20000503
BR 2000010391	A	20020702	BR 2000-10391	20000503
EE 200100589	A	20030217	EE 2001-589	20000503
NZ 514980	A	20031031	NZ 2000-514980	20000503
AU 772846	B2	20040506	AU 2000-45891	20000503
ZA 2001008971	A	20030130	ZA 2001-8971	20011030
BG 106073	A	20020531	BG 2001-106073	20011101
NO 2001005448	A	20020107	NO 2001-5448	20011107
PRIORITY APPLN. INFO.:			GB 1999-10577 A	19990508
			WO 2000-GB1697 W	20000503

OTHER SOURCE(S): MARPAT 133:362712
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; or a pharmaceutically acceptable salt thereof wherein n is 0-1; X and Y are independently selected from NH, O, S, or NR8 where R8 is alkyl of 1-6 carbon atoms and X may addnl. comprise a CH2 group; R7 is a group (CH2)mR9 where m is 0, or an integer of from 1-3 and R9 is a substituted aryl group, an optionally substituted cycloalkyl ring of up to

L6 ANSWER 30 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
10 carbon atoms, or an optionally substituted heterocyclic ring or an N-oxide of any nitrogen contg. ring; R6 is a divalent cycloalkyl of 3 to 7 carbon atoms, which may be optionally further substituted with one or more alkyl of 1 to 6 carbon atom groups; or is a divalent pyridinyl, pyrimidinyl, or Ph ring; wherein the pyridinyl, pyrimidinyl, or Ph ring may be optionally further substituted with one or more specified groups; R1, R2, R3 and R4 are each independently selected from hydrogen or various specified org. groups]. Title compds. are useful as pharmaceuticals for the inhibition of MEK activity. Thus, the title compd. II was prepd. and tested in HT29 human colon tumor cell proliferation assay.
IT **306997-87-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinoline derivs. as inhibitors of MEK enzymes)
RN 306997-87-5 CA
CN 3-Quinolinecarbonitrile, 6-methoxy-4-[[4 (2 methoxyphenoxy)phenyl]amino)-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

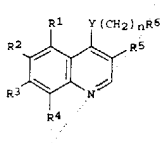


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 31 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:350152 CA
TITLE: Preparation of quinoline derivatives as inhibitors of MEK enzymes
INVENTOR(S): Gibson, Keith Hopkinson
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068200	A1	20001116	WO 2000 GB1707	20000503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000010324	A	20020108	BR 2000-10324	20000503
EP 1178966	A1	20020213	EP 2000-927497	20000503
EP 1178966	B1	20031022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103184	T2	20020321	TR 2001-200103184	20000503
NZ 514814	A	20031031	NZ 2000-514814	20000503
AT 252561	E	20031115	AT 2000 927497	20000503
ZA 2001008965	A	20030130	ZA 2001-8965	20011030
NO 2001005446	A	20011212	NO 2001-5446	20011107
PRIORITY APPLN. INFO.:			GB 1999-10579 A	19990508
			WO 2000-GB1707 W	20000503

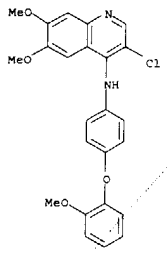
OTHER SOURCE(S): MARPAT 133:350152
GI



I

AB The title compds. I [n = 0-1; Y = NH, O, S, NR7 where R7 is alkyl of 1-6 carbon atoms; R5 = Cl, Br; Y is selected from NH, O, S, NR7 where R7 is alkyl of 1-6 carbon atoms; R6 is a specified cyclic group which may be substituted by various specified substituents, or R6 = R8XR9; R1, R2, R3, R4 = H, hydroxy, halo, cyano, nitro, trifluoromethyl, etc.], useful in the

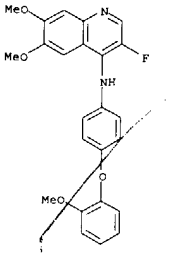
L6 ANSWER 31 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
inhibition of MEK enzymes, were prepd. E.g.,
4-(2 methoxyphenoxy)anilino
3-chloro-6,7-dimethoxyquinoline was prepd.
IT **304904-38-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline derivs. as inhibitors of MEK enzymes)
RN 304904-38-9 CA
CN 4-Quinolinamine, 3-chloro-6,7-dimethoxy-N-[4 (2-methoxyphenoxy)phenyl]-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 32 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
group R8XR9 and X is selected from CH2, NH, O, S, NR5; R1, R2, R3, R4 = H,
OH, halo, cyano, NO2, etc.], inhibitors of MEK enzymes, were prepd. E.g.,
reaction of 4-chloro-6,7-dimethoxy-3-fluoroquinoline (prepn. given) and
4-(2-methoxyphenoxy)aniline gave
4-(2-methoxyphenoxy)anilino-3-fluoro 6,7-dimethoxyquinoline.
IT **305800-85-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline derivs. as inhibitors of MEK enzymes)
RN 305800-85-5 CA
CN 4-Quinolinamine, 3-fluoro-6,7-dimethoxy-N-[4-(2-methoxyphenoxy)phenyl]-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 32 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 133:350151 CA
TITLE: Preparation of quinoline derivatives as inhibitors of MEK enzymes
INVENTOR(S): Gibson, Keith Hopkinson
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068199	A1	20001116	WO 2000-GB1698	20000503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000010366	A	20020213	BR 2000-10366	20000503
EP 1178965	A1	20020213	EP 2000-927492	20000503
EP 1178965	B1	20030924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103185	T2	20020521	TR 2001 200103185	20000503
AT 250582	E	20031015	AT 2000-927492	20000503
US 6638945	B1	20031028	US 2001-959434	20011025
ZA 2001008969	A	20030130	ZA 2001-8969	20011030
NO 2001005447	A	20011212	NO 2001-5447	20011107
PRIORITY APPLN. INFO.:			GB 1999-10580 A	19990508
			WO 2000-GB1698 W	20000503

OTHER SOURCE(S): MARPAT 133:350151
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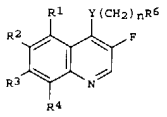
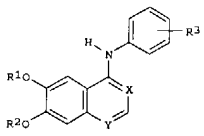


I

AB The title compds. I [n = 0-1; Y = NH, O, S, NR7 where R7 is alkyl of 1-6 carbon atoms; R6 = cycloalkyl, pyridinyl, pyrimidinyl, Ph; or R6 is a

L6 ANSWER 33 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 133:237831 CA
TITLE: 4-Anilino-6,7-dialkoxyquinoline-3-carbonitrile inhibitors of epidermal growth factor receptor kinase and their bioisosteric relationship to the 4-anilino-6,7-dialkoxyquinazoline inhibitors
AUTHOR(S): Wissner, Allan; Berger, Dan M.; Boschelli, Diane H.; Floyd, M. Brawner Jr.; Greenberger, Lee M.; Gruber, Brian C.; Johnson, Bernard D.; Mamuya, Nellie; Nilakantan, Ramaswamy; Reich, Marvin F.; Shen, Ru; Tsou, Hwei-Ru; Upeslacis, Erik; Wang, Yu Fen; Wu, Biqi; Ye, Fei; Zhang, Nan
CORPORATE SOURCE: A Division of American Home Products, Wyeth-Ayerst Research, Pearl River, NY, 10965-1215, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(17), 3244-3256
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:237831
GI



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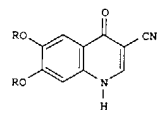


II

AB The synthesis and SAR (structure-activity relationship) of a series of 4-anilino-6,7-dialkoxyquinoline 3-carbonitrile inhibitors of epidermal growth factor receptor (EGF-R) kinase, I [R1 = Me, Et, MeOCH2, MeO(CH2)2, R2 = H, Et, MeO(CH2)2, etc.; R1R2 = CH2, CH2CH2, (CH2)3, R3 = 3-Br, 4-F, 3-NHAc, etc., X = CCO2Et, N, CCN, etc., Y = N, CCN], are described. Condensation of 3,4-dialkoxyanilines with Et (ethoxymethylene)cyanoacetate
followed by thermal cyclization gave, regiospecifically, 6,7 dialkoxy-4-oxo-1,4-dihydroquinoline-3-carbonitriles, e.g. II (R = Et, Me). Chlorination (POCl3) followed by the reaction with substituted anilines furnished the 4 anilino-6,7-dialkoxyquinoline 3-carbonitrile inhibitors of EGF-R kinase. An alternate synthesis of these compds. starts with a Me 3,4-dialkoxybenzoate. Nitration followed by redn. (Fe, NH4Cl, MeOH-H2O) gave a Me 2-amino-4,5-dialkoxybenzoate. Amidine formation using DMF-acetal followed by cyclization using LiCH2CN furnished
a 6,7-dialkoxy-4-oxo-1,4-dihydroquinoline-3-carbonitrile, which was transformed as before. Compds. contg. acid, ester, amide, carbinol, and aldehyde groups at the 3 position of the quinoline ring were also prepd. for comparison, as were several 1-anilino-6,7-dimethoxyisoquinoline-4-carbonitriles. The compds. were evaluated for their ability to inhibit the autophosphorylation of the catalytic domain of EGF-R. The SAR of these inhibitors with respect to the nature of the 6,7-alkoxy groups, the aniline substituents, and the substituent at the 3-position was studied.

L6 ANSWER 33 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

The compds. were further evaluated for their ability to inhibit the growth of cell lines that overexpress EGF-R or HER-2. It was found that 4-anilinoquinoline-3-carbonitriles are effective inhibitors of EGF-R kinase with activity comparable to the 4-anilinoquinazoline-based inhibitors. A new homol. model of EGF-R kinase was constructed based on the X-ray structures of Hck and FGF receptor 1 kinase. The model suggests that with the quinazoline-based inhibitors, the N3 atom is hydrogen-bonded to a water mol. which, in turn, interacts with Thr 830. It is proposed that the quinoline-3-carbonitriles bind in a similar manner where the water mol. is displaced by the cyano group which interacts with the same Thr residue.

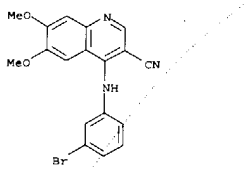
IT **214488-80-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(mol. modeling study; prepn., EGF-R kinase inhibitory activity, and structure-activity relationship of anilinoquinolinecarbonitrile derivs.)

RN 214488-80-9 CA

CN 3-Quinolinecarbonitrile, 4-[(3-bromophenyl)amino]-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 34 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 132:265207 CA

TITLE: Preparation of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors of cytokine mediated disease

INVENTOR(S): Cumming, John Graham

PATENT ASSIGNEE(S): Zeneca Limited, UK

SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

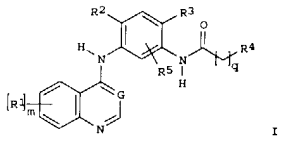
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020402	A1	20000413	WO 1999-GB3220	19990927
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2341374	AA	20000413	CA 1999-2341374	19990927
AU 9961064	A1	20000426	AU 1999-61064	19990927
AU 761552	B2	20030605		
BR 9914162	A	20010626	BR 1999 14162	19990927
EP 1117653	A1	20010725	EP 1999-947686	19990927
EP 1117653	B1	20030205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526538	T2	20020820	JP 2000-574519	19990927
AT 232205	E	20030215	AT 1999-947686	19990927
NZ 510210	A	20030630	NZ 1999-510210	19990927
PT 1117653	T	20030630	PT 1999 947686	19990927
ES 2191462	T3	20030901	ES 1999-947686	19990927
ZA 2001002187	A	20020618	ZA 2001-2187	20010315
US 6593333	B1	20030715	US 2001-787883	20010323
NO 2001001631	A	20010521	NO 2001-1631	20010330
HK 1037367	A1	20030822	HK 2001-108138	20011119
US 2003216417	A1	20031120	US 2003-441084	20030520
US 6716847	B2	20040406		

PRIORITY APPLN. INFO.:

GB 1998-21338	A	19981001
GB 1999-6564	A	19990323
WO 1999-GB3220	W	19990927
US 2001 787883	A3	20010323

OTHER SOURCE(S): MARPAT 132:265207

GI



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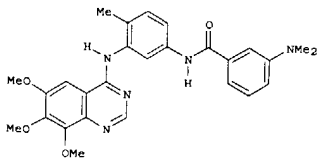


II

AB The title compds. [I; G = N, CH; R1 = OH, halo, CF3, etc.; R2, R3 = H, halo, alkyl, etc.; R4 = H, OH, alkyl, etc.; R5 = H, halo, CF3; m = 1-3; q = 0-4] and their pharmaceutically acceptable salts or in vivo cleavable esters, useful in the treatment of diseases or medical conditions mediated by cytokines, were prepd. and formulated. E.g., a multi-step synthesis of II which showed IC50 of 0.2 .mu.M against p38.alpha. kinase and IC50 of 5.2 .mu.M against TNF.alpha. prodn., was given.

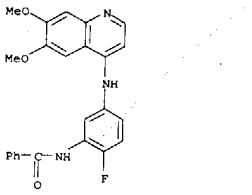
IT **263399-73-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors of cytokine mediated disease)

RN 263399-73-1 CA

CN Benzamide, N [5-[(6,7-dimethoxy-4-quinolinyl)amino] 2-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 35 OF 47 CA COPYRIGHT 2004 ACS on STN

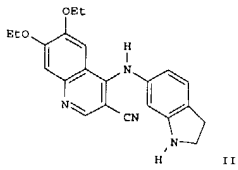
ACCESSION NUMBER: 132:265101 CA
TITLE: Preparation of 3-cyanoquinolines as protein tyrosine kinase inhibitors
INVENTOR(S): Wissner, Allan; Tsou, Hwei-Ru; Berger, Dan Maarten; Floyd, Middleton Brawner, Jr.; Hamann, Philip Ross; Zhang, Nan; Salvati, Mark Ernest; Frost, Philip
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018761	A1	20000406	WO 1999-US22054	19990922
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2344169	AA	20000406	CA 1999 2344169	19990922
AU 9961593	A1	20000417	AU 1999-61593	19990922
AU 763669	B2	20030731		
EP 1117659	A1	20010725	EP 1999-948410	19990922
EP 1117659	B1	20031203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525369	T2	20020813	JP 2000-572221	19990922
NZ 510551	A	20030328	NZ 1999-510551	19990922
AT 255575	E	20031215	AT 1999-948410	19990922
PT 1117659	T	20040430	PT 1999-948410	19990922
NO 2001001575	A	20010528	NO 2001-1575	20010328
ZA 2001002729	A	20020703	ZA 2001-2729	20010403

PRIORITY APPLN. INFO.: US 1998-162802 A 19980929
WO 1999-US22054 W 19990922

OTHER SOURCE(S): MARPAT 132:265101
GI

L6 ANSWER 35 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

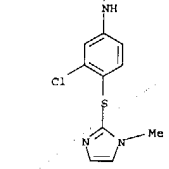


II

AB X(CH2)nZZ1CN [I; X = (un)substituted bicyclic (hetero)aryl or LTA; A = (un)substituted phenylene, -pyridinediyl, -pyrimidinediyl; T = O, S, (alkyl)imino(alkylene), oxyalkylene, etc.; Z = O, S, (alkyl or alkanoyl)imino; Z1 = 2-unsubstituted-5,6,7,8-(un)substituted quinoline-4,3-diyl; n = 0 or 1] were prepd. Thus, Me 2-amino-4,5-diethoxybenzoate was N-condensed with HCNMe2/POCl3 and the product cyclocondensed with MeCN to give, after POCl3 treatment, 4-chloro-6,7-diethoxyquinoline-3-carbonitrile which was aminated by 6-aminoindoline to give title compd II. Data for biol. activity of I were given.

IT **263170-59-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-cyanoquinolines as protein tyrosine kinase inhibitors)

RN 263170-59-8 CA
CN 3-Quinolinecarbonitrile, 4-[[3-chloro-4-[(1-methyl-1H-imidazol-2-yl)thio]phenyl]amino]-6,7-diethoxy (9CI) (CA INDEX NAME)



L6 ANSWER 35 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

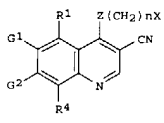
L6 ANSWER 36 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 132:265100 CA
TITLE: Preparation of substituted 3-cyanoquinolines as protein tyrosine kinases inhibitors
INVENTOR(S): Wissner, Allan; Tsou, Hwei-Ru; Berger, Dan Maarten; Floyd, Middleton Brawner, Jr.; Hamann, Philip Ross; Zhang, Nan; Frost, Philip
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018740	A1	20000406	WO 1999-US22056	19990922
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2344168	AA	20000406	CA 1999-2344168	19990922
AU 9961594	A1	20000417	AU 1999-61594	19990922
BR 9914164	A	20010626	BR 1999-14164	19990922
EP 1117649	A1	20010725	EP 1999 948411	19990922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525359	T2	20020813	JP 2000 572200	19990922
NZ 510580	A	20030328	NZ 1999-510580	19990922
ZA 2001002501	A	20020105	ZA 2001-2501	20010327
NO 2001001574	A	20010528	NO 2001-1574	20010328

PRIORITY APPLN. INFO.: US 1998-162289 A 19980929
WO 1999-US22056 W 19990922

OTHER SOURCE(S): MARPAT 132:265100
GI



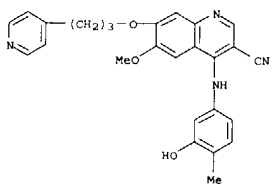
I

AB The title compds. I [X = cycloalkyl, pyridinyl, pyrimidinyl, etc.; Z = NH, O, S, NR; G1, G2, R1, R4 = H, halo, alkyl, alkynyl, etc.; n = 0,1], protein tyrosine kinase inhibitors, were prepd. E.g.,

L6 ANSWER 36 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
4-(2-methoxyethoxy)but-2-ynoic acid [4 (3-bromophenylamino)-3-cyanoquinolin-6-yl]amide was prepd. I are useful as antineoplastic agents.

IT **263149-12-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyanoquinolines as protein tyrosine kinase inhibitors)

RN 263149-12-8 CA
CN 3-Quinolinecarbonitrile, 4-[(3 hydroxy-4-methylphenyl)amino]-6-methoxy-7-[3-(4-pyridinyl)propoxy]-, hydrochloride (9CI) (CA INDEX NAME)



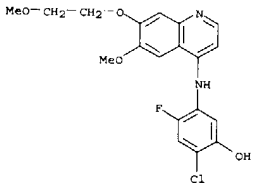
●x HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 37 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)
well with respect to potency and selectivity for inhibition of growth factor stimulated proliferation of human umbilical vein endothelial cells (HUVECs). Oral administration of selected compds. to mice produced total plasma levels 6 h after dosing of between 3 and 49 .mu.M. In vivo efficacy was demonstrated in a rat uterine edema assay where significant activity was achieved at 60 mg/kg with I [R1 = Me, R2 = OMe]. Inhibition of growth of human tumors in athymic mice has also been demonstrated: I [R1 = Br, R2 = 2-(1,2,3-triazol-1-yl)ethoxy] inhibited the growth of established Calu-6 lung carcinoma xenograft by 75% (P < 0.001, one tailed t-test) following daily oral administration of 100 mg/kg for 21 days.

IT **205447-54-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and structure-activity relationship of arylaminoquinazoline VEGF receptor tyrosine kinase inhibitors)

RN 205447-54-7 CA
CN Phenol, 2 chloro-4-fluoro-5-[[6-methoxy 7 (2-methoxyethoxy)-4-quinolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

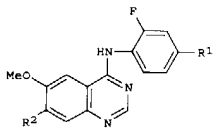


● HCl

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 37 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 132:151769 CA
TITLE: Design and Structure Activity Relationship of a New Class of Potent VEGF Receptor Tyrosine Kinase Inhibitors
AUTHOR(S): Hennequin, Laurent F.; Thomas, Andrew P.; Johnstone, Craig; Stokes, Elaine S. E.; Ple, Patrick A.; Lohmann, Jean-Jacques M.; Ogilvie, Donald J.; Dukes, Mike; Wedge, Steve R.; Curwen, Jon O.; Kendrew, Jane; Lambert van der Brempt, Christine
CORPORATE SOURCE: AstraZeneca Zeneca Pharma Centre de Recherches Z.I. La Pompelle, Reims, 51689, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(26), 5369-5389
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

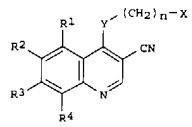
AB A series of substituted 4-anilinoquinazolines and related compds. were synthesized as potential inhibitors of vascular endothelial growth factor (VEGF) receptor (Flt and KDR) tyrosine kinase activity. Enzyme screening indicated that a narrow structure-activity relationship (SAR) existed for the bicyclic ring system, with quinazolines, quinolines, and cinnolines having activity and with quinazolines and quinolines generally being preferred. Substitution of the aniline was investigated and clearly indicated that small lipophilic substituents such as halogens or Me were preferred at the C-4' position. Small substituents such as hydrogen and fluorine are preferred at the C-2' position. Introduction of a hydroxyl group at the meta position of the aniline produced the most potent inhibitors of Flt and KDR tyrosine kinases activity with IC50 values in the nanomolar range. Investigation of the quinazoline C-6 and C-7 positions indicates that a large range of substituents are tolerated at C-7, whereas variation at the C 6 is more restricted. At C-7, neutral, basic, and heteroarom. side chains led to very potent compds., as illustrated by the methoxyethoxy deriv. I [R1 = 4-Cl, R2 = OCH2CH2OMe] (IC50 < 2 nM). These inhibitors proved to be very selective inhibitors of Flt and KDR tyrosine kinase activity when compared to that assocd. with the FGF receptor (50- to 3800-fold). Obsd. enzyme profiles translated

L6 ANSWER 38 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 132:35620 CA
TITLE: Preparation of substituted 3-cyanoquinolines as inhibitors of growth factor receptor protein tyrosine kinases (PTK)
INVENTOR(S): Wissner, Allan; Johnson, Bernard D.; Reich, Marvin F.; Floyd, Middleton B. , Jr.; Kitchen, Douglas B.; Tsou, Hwei-ru
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 80 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6002008	A	19991214	US 1998-49718	19980327
PRIORITY APPLN. INFO.:			US 1997 41963P P	19970403

OTHER SOURCE(S): MARPAT 132:35620
GI



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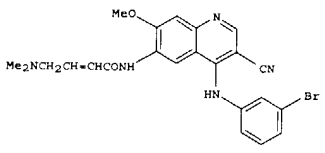


II

AB This invention provides compds. having the formula (I; wherein: X is cycloalkyl which may be optionally substituted; or is a pyridinyl, pyrimidinyl, or Ph ring; wherein the pyridinyl, pyrimidinyl, or Ph ring may be optionally substituted; n is 0-1; Y is NH, O, S, or NR; R is alkyl of 1-6 carbon atoms; R1, R2, R3, and R4 are each, independently, hydrogen, halogen, alkyl, alkenyl, alkynyl, alkenyloxy, alkynoyloxy, hydroxymethyl, halomethyl, alkanoyloxy, alkenoyloxy, alkynyloxy, alkanoyloxymethyl,

L6 ANSWER 38 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

alkenoyloxymethyl, alkynoyloxymethyl, alkoxymethyl, alkoxy, alkylthio, alkylsulphinyl, alkylsulfonyl, alkylsulfonamido, alkenylsulfonamido, alkynylsulfonamido, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy, carboalkyl, phenoxy, Ph, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino, alkylamino, dialkylamino, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, phenylamino, benzylamino, etc.; R5 is alkyl which may be optionally substituted, or Ph which may be optionally substituted; R6 is hydrogen, alkyl, or alkenyl; R7 is chloro or bromo; R8 is hydrogen, alkyl, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, N-cycloalkylaminoalkyl, N-cycloalkyl-N-alkylaminoalkyl, N,N-dicycloalkylaminoalkyl, morpholino-N-alkyl, piperidino-N-alkyl, N-alkyl-piperidino-N-alkyl, azacycloalkyl-N-alkyl, hydroxyalkyl, alkoxyalkyl, carboxy, carboalkoxy, Ph, carboalkyl, chloro, fluoro, or bromo; Z is amino, hydroxy, alkoxy, alkylamino, dialkylamino). The compds. of the present invention inhibit the action of certain growth factor receptor protein tyrosine kinases (PTK) thereby inhibiting the abnormal growth of certain cell types. They are therefore useful for the treatment of certain diseases that are the result of deregulation of these PTKs, in particular as anti-cancer agents for the treatment of cancers expressing epidermal growth factor receptor (EGFR), mitogen activated protein kinase (MAPK), epithelial kinase (ECK), and kinase insert domain contg. receptor (KDR) in mammals and for the treatment of polycystic kidney disease in mammals. Thus, To a mixt. of 1.9 g (5.1 mmol) of 4-[(3-bromophenyl)amino]-7-methoxy-6-amino-3-quinolinecarbonitrile and 5.3 mL (31 mmol) of Hunig's base in 110 mL of dry THF at 0.degree. C., with stirring, was added a THF soln. contg. 5.7 g (31 mmol) of 4-bromocrotonyl chloride dropwise. The mixt. was stirred for addnl. 0.5 h. After addn. 100 mL of satd. sodium chloride soln. was added to the reaction mixt., then it was extd. with Et acetate. The Et acetate soln. was dried over sodium sulfate and then was added to 40 mL of di-Me amine soln. (2.0 M in THF) at 0.degree. dropwise and stirred an addnl. 0.5 h to give 4-Dimethylamino but-2-enoic acid [4-(3-bromo-phenylamino)-3-cyano-7-methoxy quinolin-6-yl]amide (II). II showed IC50 of 0.000008 .mu.M against epidermal growth factor receptor kinase.

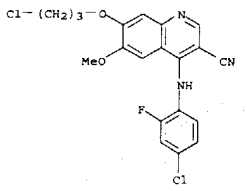
IT **214484-54-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of substituted 3-cyanoquinolines as inhibitors of growth factor receptor protein tyrosine kinases (PTK) for treatment of cancers and polycystic kidney disease)

RN 214484-54-5 CA

CN 3-Quinolinecarbonitrile, 4-[(4-chloro-2-fluorophenyl)amino]-7-(3-chloropropoxy)-6-methoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 38 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 39 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 131:58896 CA

TITLE: A simple synthesis of 3-phosphonyl-4-aminoquinolines from .beta.-enaminophosphonates

AUTHOR(S): Palacios, Francisco; Ochoa de Retana, Ana; Oyarzabal, Julen

CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Farmacia, Universidad del Pafs Vasco, Vitoria, 01080, Spain

SOURCE: Tetrahedron (1999), 55(18), 5947-5964
CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:58896

AB An easy and efficient synthesis of 4-aminoquinolines substituted with a phosphorylated group or a phosphine oxide group in the 3-position is described. The key step is a regioselective addn. of lithiated .beta.-enamino phosphonates to isocyanates to give functionalized amides. Subsequent cyclization of these compds. with PPh3 and hexachloroethane in the presence of NEt3 afforded substituted 4-aminoquinolines. The deprotection of N-PMP substituted 4-amino-quinolines with CAN in MeCN gave primary 4-aminoquinolines.

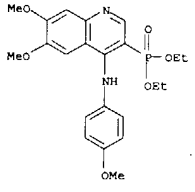
IT **228249-12-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of amides from regioselective addn. of lithiated .beta.-enamino phosphonates to isocyanates)

RN 228249-12-5 CA

CN Phosphonic acid, [6,7-dimethoxy-4-[(4-methoxyphenyl)amino]-3-quinolinyl]-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 40 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 129:302564 CA

TITLE: Preparation of substituted 3-cyanoquinolines as inhibitors of protein tyrosine kinase

INVENTOR(S): Wissner, Allan; Johnson, Bernard Dean; Reich, Marvin Fred; Floyd, Middleton Brawner, Jr.; Kitchen, Douglas B.; Tsou, Hwei-ru

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843960	A1	19981008	WO 1998-US6480	19980402
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CN 1161330	A	19971008	CN 1997-101099	19970204
ZA 9802771	A	19991001	ZA 1998-2771	19980401
AU 9868777	A1	19981022	AU 1998-68777	19980402
AU 750906	B2	20020801		
EP 973746	A1	20000126	EP 1998-914417	19980402
EP 973746	B1	20030924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 9902946	T2	20000321	TR 1999-9902946	19980402
JP 2001519788	T2	20011023	JP 1998-541981	19980402
RU 2202551	C2	20030420	RU 1999-123060	19980402
CN 1121391	B	20030917	CN 1998-805734	19980402
BR 9808478	A	20030930	BR 1998-8478	19980402
AT 250583	E	20031015	AT 1998-914417	19980402
PT 973746	T	20040227	PT 1998 914417	19980402
NO 9904798	A	19991124	NO 1999-4798	19991001
MX 9909091	A	20000831	MX 1999-9091	19991004
HK 1024917	A1	20040102	HK 2000-104179	20000707

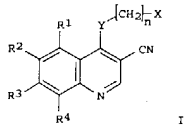
PRIORITY APPLN. INFO.: US 1997-826604 A 19970403

WO 1998-US6480 W 19980402

OTHER SOURCE(S): MARPAT 129:302564

GI

L6 ANSWER 40 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



I

AB The title compds. [I; X = (un)substituted cycloalkyl, pyridinyl, pyrimidinyl, Ph; n = 0-1; Y = NH, O, S, NR; R = = C1-6 alkyl; R1-R4 = H, halo, alkyl, etc. (with the proviso that when Y = NH; R1-R4 = H; n = 0; X is not 2-methylphenyl)], inhibitors of protein tyrosine kinase which are useful in treating, inhibiting the growth of, or eradicating a neoplasm which expresses EGFR, MAPK, ECK or KDR, and in treating polycystic kidney disease, were prepd. Thus, treatment of 2-butynoic acid with iso-Bu chloroformate and N-methylmorpholine in THF followed by the addn. of this soln. of the mixed anhydride to a soln. of 6-amino-4-[(3-bromophenyl)amino]-7-methoxy-3-quinolinecarbonitrile (prepn. described) in THF over a 24 h period afforded I [Y = NH; n = 0; X = 3-BrC6H4; R1 = R4 = H; R2 = MeC.tplbond.CC(O)NH; R3 = MeO] which showed IC50 of 0.15 .mu.M against epidermal growth factor receptor kinase (A431 membrane ext.).

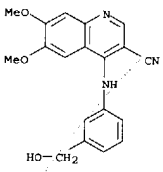
IT **214484-34-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of substituted 3-cyanoquinolines as inhibitors of protein tyrosine kinase)

RN 214484-34-1 CA

CN 3-Quinolinecarbonitrile, 4-[[3-(hydroxymethyl)phenyl]amino]-6,7-dimethoxy (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 41 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 128:270546 CA

TITLE: Quinoline derivatives inhibiting the effect of growth factors such as VEGF

INVENTOR(S): Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Ple, Patrick Alan

PATENT ASSIGNEE(S): Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Ple, Patrick Alan

SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

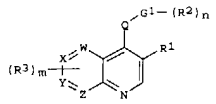
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9813350	A1	19980402	WO 1997-GB2587	19970923
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2263479	AA	19980402	CA 1997-2263479	19970923
AU 9743137	A1	19980417	AU 1997-43137	19970923
AU 733551	B2	20010517		
EP 929526	A1	19990721	EP 1997-941115	19970923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1237963	A	19991208	CN 1997-199929	19970923
JP 2001500890	T2	20010123	JP 1998-515386	19970923
NO 9901423	A	19990511	NO 1999-1423	19990324
KR 2000048575	A	20000725	KR 1999-702502	19990324
PRIORITY APPLN. INFO.:			EP 1996-402034 A	19960925
			WO 1997-GB2587 W	19970923

OTHER SOURCE(S): MARPAT 128:270546

GI

L6 ANSWER 41 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



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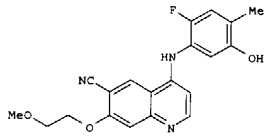


II

AB The invention relates to the use of compds. I [R1 = F or H; R2 = OH, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, CF3, cyano, amino, or NO2; n = 0-5; Q = O, NH, S, or CH2; G1 = Ph or 5- to 10-membered heteroarom. cyclic or bicyclic contg. O, S, and/or N; W, X, Y, Z = CH or N (but all 4 .noteq. N); m = 1-3; R3 = H, OH, halo, cyano, NO2, CF3, C1-3 alkyl, NR4R5 (wherein R4 and R5 = H or C1-3 alkyl), or R6X1 wherein X1 = CH2 or heteroatom linker group, and R6 = alkyl, alkenyl or alkynyl chain (un)substituted by OH, amino, NO2, alkyl, cycloalkyl, alkoxyalkyl, (un)substituted pyridone, Ph, heterocyclyl, etc. (which alkyl, alkenyl or alkynyl chain may have heteroatom linker), or R6 = (un)substituted pyridone, Ph, or heterocyclyl], and salts thereof, in the manuf. of medicaments for prodn. of an antiangiogenic and/or vascular permeability-reducing effect. Also disclosed are processes for the prepn. of I, and pharmaceutical compns. contg. them as active ingredients. I and salts inhibit the effects of VEGF, a property useful in the treatment of a no. of disease states including cancer and rheumatoid arthritis (no data). Examples include 63 syntheses and 7 general formulations. For instance, condensation of 4-chloro-6-cyano-7-(2-methoxyethoxy)quinoline hydrochloride with 2-fluoro-5-hydroxy-4-methylaniline (prepns. given) in refluxing iso-PrOH gave 68% title compd. II, isolated as the HCl salt.

IT **205448-49-3P**

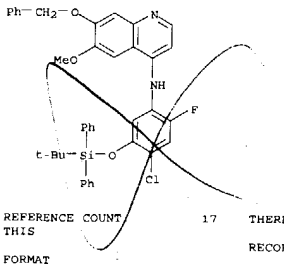
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of quinoline derivs. as growth factor inhibitors)

RN 205448-49-3 CA

CN 4-Quinolinamine, N-[4-chloro-5-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2-fluorophenyl]-6-methoxy-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

L6 ANSWER 41 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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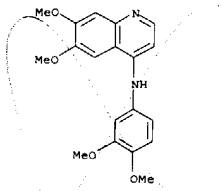
L6 ANSWER 42 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 128:162549 CA
TITLE: A novel series of 4-phenoxyquinolines: potent and highly selective inhibitors of PDGF receptor autophosphorylation
AUTHOR(S): Kubo, Kazuo; Shimizu, Toshiyuki; Ohyama, Shin-Ichi; Murooka, Hideko; Nishitoba, Tsuyoshi; Kato, Shinichiro; Kobayashi, Yoshiko; Yagi, Mikio; Isoe, Toshiyuki; Nakamura, Kazuhide; Osawa, Tatsushi; Izawa, Toshio
CORPORATE SOURCE: Pharmaceutical Research Laboratory, KIRIN Brewery Co., Ltd., Takasaki, 370-12, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(23), 2935-2940
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel series of 4-phenoxyquinolines, some of which showed potent and highly selective inhibitory activities for PDGF receptor autophosphorylation, was discovered. Interestingly, their structures were very similar to those of the selective inhibitors for EGF receptor autophosphorylation.
IT **202917-10-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(4-phenoxyquinolines as potent and highly selective inhibitors of PDGF receptor autophosphorylation)
RN 202917-10-0 CA
CN 4-Quinolinamine, N (3,4-dimethoxyphenyl)-6,7-dimethoxy (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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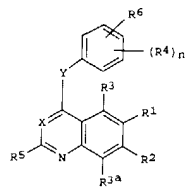
L6 ANSWER 42 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

L6 ANSWER 43 OF 47 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 125:114665 CA
TITLE: Preparation of quinoline and quinazoline protein tyrosine kinase inhibitors
INVENTOR(S): Hudson, Alan Thomas; Vile, Sadie; Barraclough, Paul; Franzmann, Karl Witold; McKeown, Stephen Carl; Page, Martin John
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9609294	A1	19960328	WO 1995-GB2202	19950918
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9534824	A1	19960409	AU 1995-34824	19950918
ZA 9507853	A	19970318	ZA 1995-7853	19950918
EP 782570	A1	19970709	EP 1995-931351	19950918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10505600	T2	19980602	JP 1995-509740	19950918

PRIORITY APPLN. INFO.: GB 1994-18852 A 19940919
GB 1995-7788 A 19950413
GB 1995-10757 A 19950526
WO 1995-GB2202 W 19950918

OTHER SOURCE(S): MARPAT 125:114665
GI



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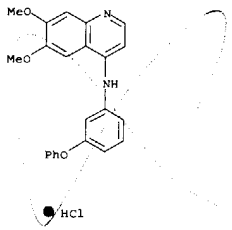
L6 ANSWER 43 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

AB The title compds. [I; X = N, CH; Y = W(CH2), (CH2)W, W; W = O, S(O)m, (un)substituted NH; R1 = NH2, H, halogen, OH, NO2, CO2H, CF3, CF3O, ureido, etc.; R4 = H, OH, halogen, alkyl, alkoxy, alkylthio, CN, NO2, CF3, etc.; n = 1-3; R5 = H, halogen, CF3, alkyl, alkoxy; R6 = substituted hydrocarbyl, etc.], which are protein tyrosine kinase inhibitors, are prepd. Thus, 4-chloroquinoline was reacted with 4-methoxyaniline in the presence of HCl, producing 4-(4-phenoxyanilino)quinoline hydrochloride, m.p. 216-218.degree., which demonstrated a IC50 against p56lck protein tyrosine kinase of 5 .mu.M.

IT **179246-08-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline and quinazoline protein tyrosine kinase inhibitors)

RN 179246-08-3 CA

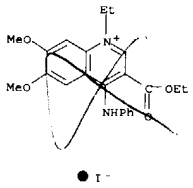
CN 4 Quinolinamine, 6,7-dimethoxy-N (3-phenoxyphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



L6 ANSWER 44 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

RN 65937-58-8 CA

CN Quinolinium, 3-(ethoxycarbonyl)-1-ethyl-6,7-dimethoxy-4-(phenylamino)-, iodide (9CI) (CA INDEX NAME)



L6 ANSWER 44 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 92:215236 CA

TITLE: Studies on quinoline derivatives and related compounds. VI. A novel displacement reaction of 1-ethylquinolinium iodides with nucleophiles

AUTHOR(S): Agui, Hideo; Nakagome, Takenari

CORPORATE SOURCE: Pharm. Div., Sumitomo Chem. Co., Takarazuka, 665, Japan

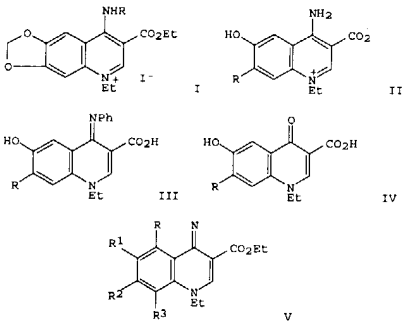
SOURCE: Journal of Heterocyclic Chemistry (1979), 16(7), 1353-60
CODEN: JHTCAD; ISSN: 0022-152X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 92:215236

GI



AB The reaction of 4-amino- and 4-anilino-3 carbethoxy-1-ethyl 6,7-(methylenedioxy)quinolinium iodide I (R = H, Ph, resp.) with nucleophiles produced 7-substituted 4-amino-3-carboxy-1-ethyl-6-hydroxyquinolinium betaines II (R = OMe, OEt, SEt) and 7 substituted 1-ethyl 1,4-dihydro-6-hydroxy 4-(phenylimino)-3-quinolinecarboxylic acids III (same R), resp., which led to 7-substituted 1-ethyl-1,4-dihydro 6-hydroxy-4-oxo-3 quinolinecarboxylic acids IV by alk. hydrolysis. These novel displacements were attempted with a variety of 1-ethyl-1,4-dihydroquinolinecarboxylates V (R, R1, R3 = H, OMe; R = H, OMe, Cl, SMe).

IT **65937-58-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with ethanolic potassium hydroxide)

L6 ANSWER 45 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 88:121005 CA

TITLE: 7-Alkoxy(or alkylthio)-1-ethyl-1,4-dihydro-4 imino-3-quinolinecarboxylic acids

INVENTOR(S): Agui, Hideo; Nakagome, Takenari

PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 52142076	A2	19771126	JP 1976 59300	19760521
PRIORITY APPLN. INFO.:			JP 1976-59300	19760521

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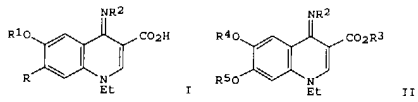
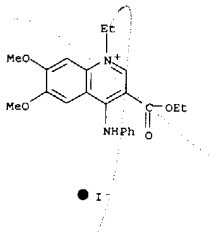


AB Title acids I (R = OMe, OEt, SEt; R1 = H, Me; R2 = H, Ph) were prepd. by heating II (R3 = H, Et; R4 = R5 = Me or R4R5 = CH2) with MeOH, EtOH, or EtSH in the presence of KOH. Thus, 0.17 g II (R2 = Ph, R3 = H, R4R5 = CH2) was refluxed with 0.066 g 85% KOH in EtOH for 6 h to give 0.15 g I (R = EtO, R1 = H, R2 = Ph).

IT **65937-58-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 65937-58-8 CA

CN Quinolinium, 3-(ethoxycarbonyl)-1-ethyl-6,7-dimethoxy-4-(phenylamino)-, iodide (9CI) (CA INDEX NAME)



L6 ANSWER 45 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)

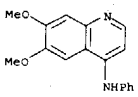
L6 ANSWER 46 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 76:42038 CA
TITLE: Synthesis and hypotensive properties of new 4-aminoquinolines
AUTHOR(S): Wright, George C.; Watson, Edward J.; Ebetino, Frank F.; Lougheed, Guy; Stevenson, Benjamin F.; Winterstein, Alexander; Bickerton, Robert K.; Halliday, Robert P.; Pals, Donald T.
CORPORATE SOURCE: Chem. Div., Norwich Pharmacal Co., Norwich, NY, USA
SOURCE: Journal of Medicinal Chemistry (1971), 14(11), 1060-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fifty-nine 4-substituted quinolines were synthesized and tested for hypotensive activity in dogs. Of 41 simple 4 (alkylamino)-6,7-dimethoxyquinolines (I), 11 compds. exhibited good hypotensive activity, equal to that of the parent 4-amino-6,7-dimethoxyquinolin (I, R = NH2) [1696-79 3]. The I iodides were prepd. by displacement of the corresponding 4-chloroquinolines with amines in PhOH, followed by alkylation and had decreased activity as compared with the I.

IT **2004-34-4**
RL: BIOL (Biological study)
(antihypertensive)

RN 2004-34-4 CA
CN 4-Quinolinamine, 6,7-dimethoxy-N-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 47 OF 47 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 63:3284 CA
ORIGINAL REFERENCE NO.: 63:589b-e
TITLE: 4-Amino-6,7-dialkoxyquinolines
INVENTOR(S): Ebetino, Frank F.; Wright, George C.
PATENT ASSIGNEE(S): Norwich Pharmacal Co.
SOURCE: 27 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1388756		19650212	FR	
BE 640817			BE	
DE 1202280			DE	
GB 1010254			GB	
NL 300630			NL	
US 3272824		1966	US	
PRIORITY APPLN. INFO.:			US	19621206

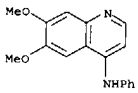
GI For diagram(s), see printed CA Issue.

AB The title compds., hypotensive agents, are prepd. according to the given equation, where R and R1 are OCH3; R2 is H, or CH3; and R3 is H, NH2, lower alkyl, hydroxyalkyl, alkoxy, carbethoxymethyl, aminoalkyl, dialkyl, acetyl, benzyl, phenyl, or cyclohexyl groups. Also R2 and R3 together may constitute the atoms necessary to complete a cyclic system forming morpholine or N-methylpiperazine. For example, a suspension of 5 g. 4-chloro-6,7-dimethoxyquinoline in 20 ml. hydrazine hydrate (100%) is refluxed 75 min., the soln. cooled and filtered, the ppt. washed with H2O and recrystd. twice from 5% HCl, giving 21% yield 4-hydrazino-6,7-dimethoxyquinoline, m. 283-8.degree.. Similarly prepd. were the following 6,7-dimethoxyquinolines (substituents given): 4-amino, HCl salt m. 274-6.degree. (EtOHH2O); 4-methylamino, HCl salt m. 268-70.degree. (decompn.); 4-(2-ethoxyethylamino), m. 190-3.degree. (iso-PrOH); 4-(2-hydroxyethylamino), HCl salt m. 233-6.degree. (MeOH); 4-(2-hydroxyethylamino), HCl salt m. 233-6.degree. (MeOH); 4-benzylamino, HCl salt m. 248-9.degree. (MeOH); 4-(4'-methylpiperazino), di-HCl.H2O salt m. 240-6.degree. (decompn.) (MeOH); 4-dimethylamino, HCl.0.5H2O salt m. 244-5.degree. (EtOH); 4-isopropylamino, HCl salt m. 242 4.degree. (EtOH); 4-anilino, HCl salt m. 247 50.degree.; 4-(3-hydroxypropylamine), HCl salt m. 235-6.degree. (MeOH); 4-amino-2-ethylamino, di-HCl.2H2O salt, m. 245-6.degree. (MeOH); 4-morpholino, HCl.H2O salt m. 210 13.degree. (EtOH); 4 (3-methoxypropylamino), HCl salt m. 225-8.degree. (EtOH); 4-cyclohexylamino, HCl.0.5H2O salt m. 241-2.degree.; 4-pentylamino, HCl.0.5H2O salt m. 198-200.degree. (acetonitrile); 4-acetamido, HCl.H2O salt m. 254-9.degree. (EtOH); 4-ethylglycinate, HCl.0.5H2O salt m. 224-6.degree. (iso-PrOH); 4-(2-dimethylaminoethylamino), di HCl.H2O salt m. 261-5.degree. (iso-PrOH) (decompn.). 4-Amino-6,7-diethoxyquinoline-HCl m. 273 4.degree. (EtOH).

IT **2004-34-4**, Quinoline, 4-anilino 6,7-dimethoxy-, hydrochloride
(prepn. of)

RN 2004-34 4 CA
CN 4 Quinolinamine, 6,7-dimethoxy N-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

L6 ANSWER 47 OF 47 CA COPYRIGHT 2004 ACS on STN (Continued)



● HCl

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L2            0 S L1 SAM
L3            0 S L1 FULL
L4              STRUCTURE UPLOADED
L5         1106 S L4 FULL

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L6           47 S L5

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---Logging off of STN---


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Executing the logoff script...


=> LOG Y

STN INTERNATIONAL LOGOFF AT 13:29:42 ON 22 SEP 2004
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